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VOLUME 32

JULY—DECEMBER, 1936

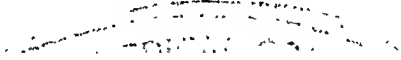
ST. LOUIS

THE C. V. MOSBY COMPANY

1936

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Printed in U. S. A.



Press of
The C. V. Mosby Company
St. Louis

American Journal of Obstetrics and Gynecology

Published by the American College of Obstetricians and Gynecologists
Vol. 32 JULY, 1936 No. 1
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Original Communications

HISTOPATHOLOGY AND TREATMENT OF VAGINITIS*

I. HISTOPATHOLOGY

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II. BIOCHEMICAL APPROACH IN TREATMENT

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PART I

HISTOPATHOLOGY OF VAGINITIS

A STUDY of the histopathology of the inflammatory diseases of the vagina presupposes some familiarity with the normal appearance of vaginal smears, including the microscopic picture of the cells and bacteria, with the appearance of the vaginal walls, especially the epithelial and sub-epithelial layers, and with some of the microchemical changes, especially those associated with the deposition of keratohyaline and glycogenic granules.

It must be recognized that there are normal age and cyclic changes in the vaginal walls associated with puberty, the menstrual cycle, pregnancy, and the menopause whether artificial or physiologic. The physiologic changes following the menopause gradually affect both the epithelial and subepithelial layers. All of the alterations are sig-

*Read at the Seventh Annual Meeting of the Central Association of Obstetricians and Gynecologists, held at Omaha, Neb., October 10 to 12, 1935.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

nified by changes in the secretions and exfoliated epithelium found in the vaginal spreads. Microchemical changes in the keratohyaline and glycogenic granules may also be seen. The normal structural variations characteristic of age and cycles are reflections of physiologic changes and adaptations to meet varying requirements.

The name of Papanicolaou is definitely associated with intensive studies of the histologic and cyclic changes in vaginal spreads and epithelium. These are so definite in some animals, especially rodents, that the microscopic picture can be used as a means of biologic tests. The essential variation is in the relative numbers of epithelial and leucocytic elements. The former with unstainable nuclei predominate at the height of estrus while the latter are in great abundance during the diestrus. This variation is associated with changes in the vaginal wall characterized by epithelial proliferation and keratinization followed by sloughing associated with heavy leucocytic infiltration. Eight or ten years ago we attempted unsuccessfully to demonstrate corresponding changes in vaginal smears from women. Papanicolaou by careful daily study of smears believes he is able to find characteristic cellular changes during menstruation, pregnancy, and the puerperium.

The normal vaginal secretion, since there are no vaginal glands, consists of a transudation of exfoliated epithelium, a few diapedetic cells, secretions from the cervix and a normal bacterial flora dominated during the period of sexual maturity by the vaginal bacillus. Studies of the age and cyclic changes in the vaginal walls have been more successful. The structural variations associated with infancy, childhood, maturity, and postmaturity have been well known for years, but the causative factor has only recently been discovered in the physiologic changes associated with hormonal activities. Before and after the period of reproductive life, the flora is similar but differs from that during maturity in that there is a prevalence of coccoid types.

The age changes are mainly those of growth and development. During infancy and childhood the vaginal walls are immature and the epithelial layer is relatively thin with slight papillary development and comparatively little tendency to keratinization. During pubescence there is a transition to the mature vaginal wall which resembles skin except for the absence of the cornified layer and the accessory skin structures. These various layers can be recognized as an epidermis about 150 to 200 microns thick which consists of the stratum corneum, the incidum, the granulosum and the malpighian or germinativum under which lies the basement membrane (Fig. 1). During menstrual and other cyclic changes, a thin keratohyaline cell layer develops in the mid-epithelial zone. The derma, or subepithelial layer, consists of a papillary and a reticular layer. Underneath it all lies the hypodermis. A description of the connective, elastic and muscular tissues is not pertinent at this time.

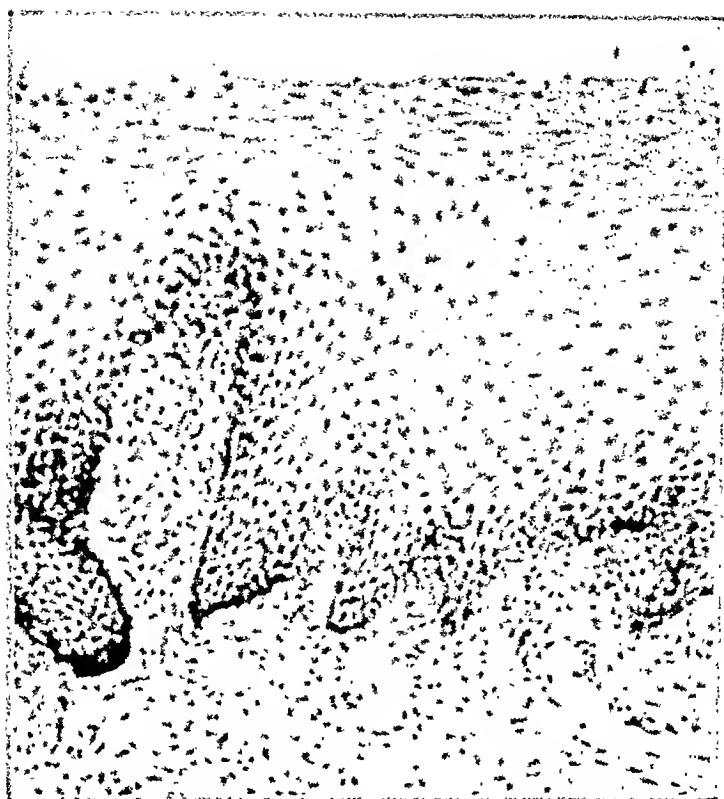


FIG. 1.—(No. 40243.) Patient, aged thirty-seven. Biopsy taken three days after menstrual period. Normal vaginal epithelial and subepithelial layers. $\times 215$.

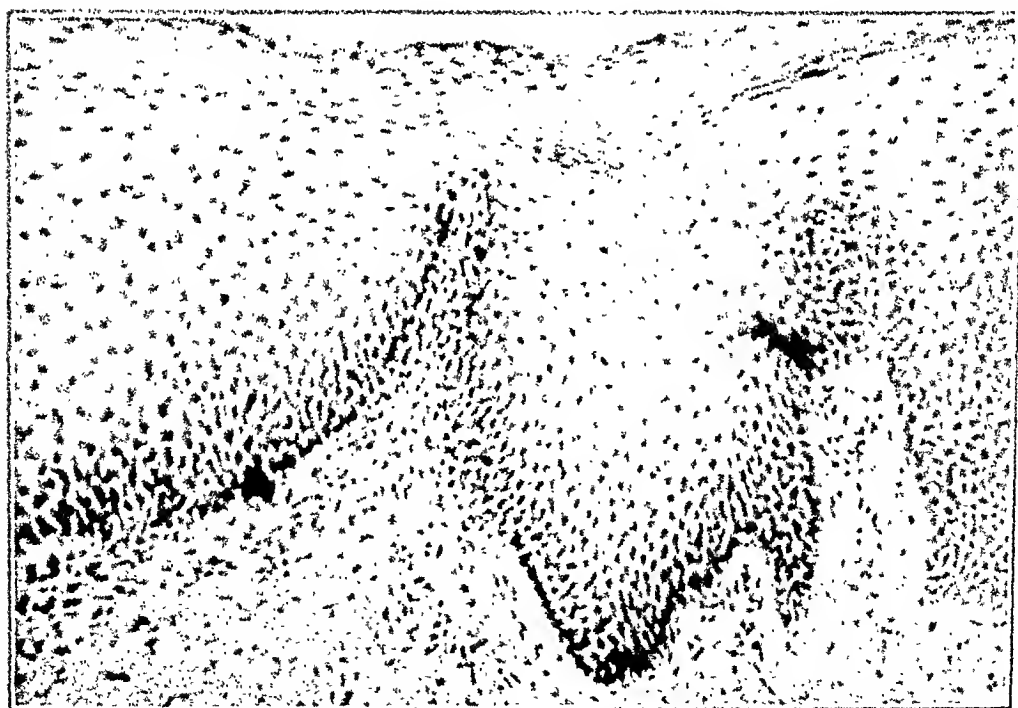


FIG. 2.—(No. 40324.) Patient, aged twenty-three, gravida iv. Biopsy taken at five lunar months. Normal epithelial and subepithelial layers. $\times 215$.

During pregnancy there are marked changes in all layers with hyperplasia and hypertrophy and an increase of tissue fluids both intravascular and extravascular (Fig. 2).

The transition through the menopause is gradual and results from atrophic changes. The folds smooth out, the epithelial layer becomes thinner, the papillary layer is less marked. The subepithelial tissues become more compact with the increase of connective tissue. There is a progressive obliteration of the vessels and an ultimate hyaline degeneration of their walls (Fig. 3).

Hitschmann and Adler (1908) clarified the morphology of the endometrial menstrual cycle and Dierks (1927) laid some foundations for further study of cyclic changes in the vaginal mucosa. He recognizes three layers: basal, functional, and

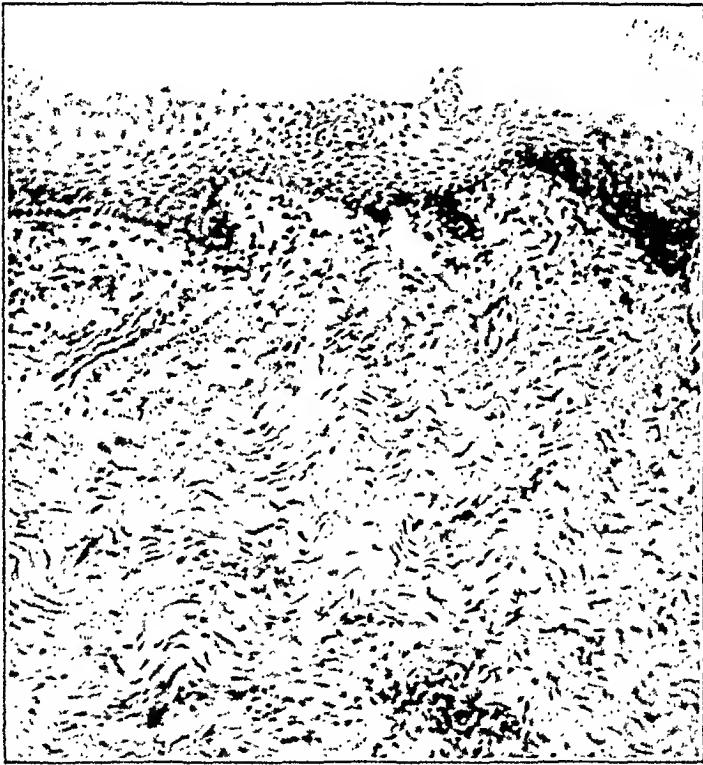


Fig. 3.—(No. 81905.) Patient, aged sixty-one. Biopsy taken at operation for cystocele and rectocele. Normal postmenopausal epithellum and subepithellum. $\times 215$.

cornifying. There is a thickening of the functional layer following menstruation, the deposition of keratohyaline, in the midportion of the zone of cornification, occurring and separating the functional from the basal layer. This is called the intraepithelial zone of cornification. During menstruation there is loss of the functional and intraepithelial layers which denudes the basal layer. Davis and Hartman have studied biopsy specimens obtained from the vaginas of monkeys and described the cyclic changes which are characterized by the greatest thickness of the epithelial layer during the midinterval. Exfoliation begins following ovulation and leads to partial loss of the functional and Dierks' layers. Cell proliferation follows along with menstruation.

Early in pregnancy the epithelial layer appears the same as during ovulation. Cells are cast off from the functional layer in increasing numbers, especially after midpregnancy, so that at the end only a

basalis of irregular thickness remains. The epithelium is completely restored at the end of the first month of the puerperium. It is probable that analogous changes take place in the woman.

Certain chemical changes undoubtedly occur in the tissues themselves. These are difficult to evaluate but certain changes in keratohyaline and glycogenic deposits can be made out by microchemical methods. The vaginal fluid has certain chemical reactions which are considered to be normal and are brought about and varied by the reaction of the transuded fluid on the admixture with the alkaline cervical secretion and with the menstrual fluid and by the action of bacteria upon these fluids. Abundant glycogen is probably present in the exfoliated cells and is broken down by the action of enzymes so that lactic acid is formed. The vaginal bacillus is normally asso-



FIG. 4. (No. 12576). Patient, no. 1 twenty-two, slide 1. Smear taken at five and one-half hour month. Vaginal bacilli predominate. $\times 2500$.

ciated with this reaction. The vaginal fluid seems to be acid from birth, though glycogen apparently disappears shortly after birth to reappear with puberty. Its presence at birth and its subsequent disappearance is doubtless due to the same hormonal influence which produces the postnatal genital involution. During childhood the pH of the vaginal fluid is about 6 to 7. During sexual maturity, it is about 4 to 4.5 except that during the menstrual period, and during the puerperium, it approaches the point of alkalinity. After the menopause, the glycogen diminishes or disappears, there is a change in the flora, and the acidity diminishes.

The discussion of the histopathology of vaginitis will be limited in this presentation to that of trichomoniasis, of mycosis and of the senile or atrophic forms.

Our observations of the two former have been made during sexual maturity. It must, of course, be remembered that the microscopic appearance is modified not only by the pathologic process but also by certain cyclic changes in the vaginal membrane which as yet are not thoroughly known. The inflammatory reactions are easily seen, and

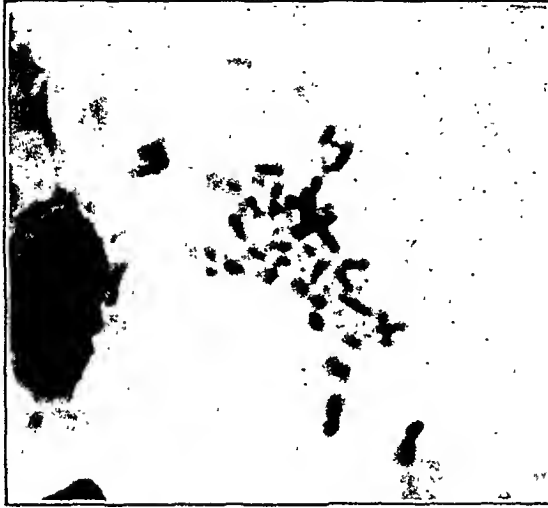


Fig. 5.—(No. 93881.) Patient, aged thirty-two. Smear taken sixth day postmenstrual from a case of trichomoniasis. Coccoid type of bacteria predominate. $\times 2500$.

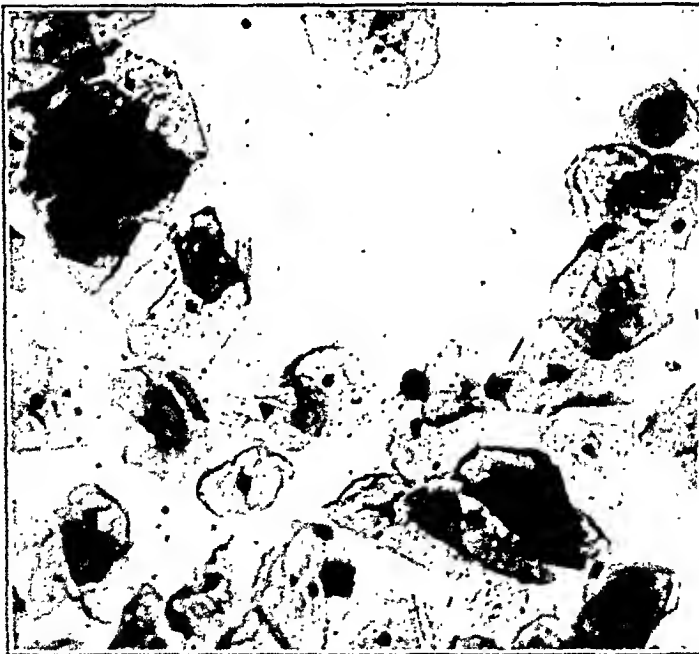


Fig. 6.—(No. 9469.) Patient, aged twenty-six, gravida II. Nephritis in previous pregnancy. Smear taken at beginning of fourth lunar month. Normal vaginal smear, some artifacts present. $\times 215$.

it is especially interesting not only to see the microscopic changes but also to note the tissue changes which occur following the treatment to be described in this contribution.

The normal vaginal flora, as seen in smears, may be divided into types. The first shows the dominant vaginal bacillus (Fig. 4), the

second exhibits coccoid forms with an admixture of the vaginal bacillus (Fig. 5), and the third shows mixed bacterial forms with the typical bacillus absent. A fourth form in which a single pathogenic organism is dominant may be recognized.

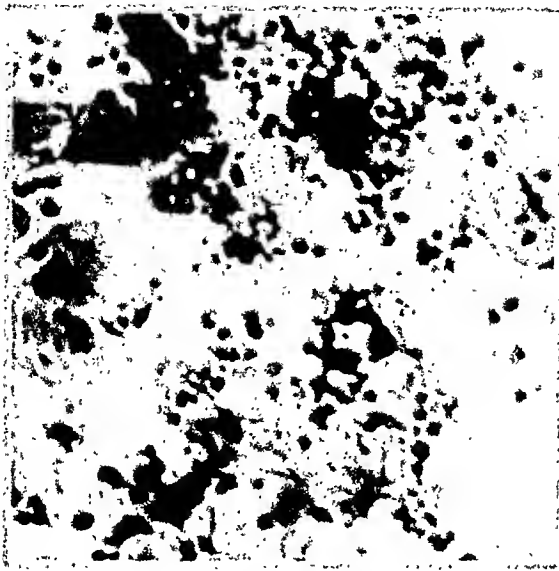


Fig. 7.—(No. 45981.) Patient, aged thirty-two. Smear taken six days after onset of illness, before treatment. $\times 240$.



Fig. 8.—(No. 45981.) Patient, aged twenty-one, gravida II. Biopsy taken at six and one-half lunar months from case of vaginal mycosis before treatment. Necrosis of superficial epithelium and leucocytic infiltration of subepithelium. $\times 210$.

The cellular content varies in these different types. Squamous epithelial cells are almost exclusively present in the first (Fig. 6), and large numbers of leucocytes together with varying numbers of epithelial cells appear in the other types (Fig. 7). In more acute inflam-

mations the leucocytes may be seen almost exclusively. In mycotic vaginitis the characteristic forms of yeastlike organisms are seen in the smears with their conidia or buds and usually with mycelia. Epithelial cells and numerous leucocytes are found. Biopsies from the vaginal walls reveal marked leucocytic infiltration of the subepithelial, deep and superficial epithelial layers with, in some instances (Fig. 8), ultimate destruction and more or less sloughing of the superficial epithelium. The associated tissue changes are characteristic of inflammations. The types of migratory cells and the character of tissue and vascular changes vary with the acuteness of the process. Aside



Fig. 9.—(No. 116285.) Patient, aged thirty-seven. Artificial menopause five years previously. Biopsy taken from case of trichomoniasis before treatment. Marked leucocytic infiltration of epithelial and subepithelial layers. $\times 125$.

from the presence of the yeastlike organisms we have found no picture which is pathognomonic of this infection.

Hanging drop preparations from patients with trichomoniasis exhibit not only the trichomonads but also numerous pus cells and bacterial forms with relatively few epithelial elements. The tissue obtained by biopsy shows the usual type of inflammatory reaction with marked leucocytic infiltration in the papillary and epithelial layers (Fig. 9). The cells in the latter undergo more or less degeneration and the superficial layers are exfoliated to a greater or less depth. In some instances the reaction is so severe in local areas as to form an almost solid wall of leucocytes in the hypodermic, dermal, and epithelial

layers. We have seen definite bacterial invasion of the superficial layers; these organisms were small, either coccoid or bacillary types, and have not been identified.

The reparative process will be discussed with senile vaginitis (Fig. 10).

Senile or atrophic vaginitis may occur in patients following an artificial as well as the normal menopause. As in other forms of vaginitis the inflammatory reaction is not uniform throughout the entire vaginal wall. Probably in this type of vaginitis there is even greater variation and tendency to involvement of rather sharply defined areas than there is in other forms except in those which are characterized by a localized ulceration.

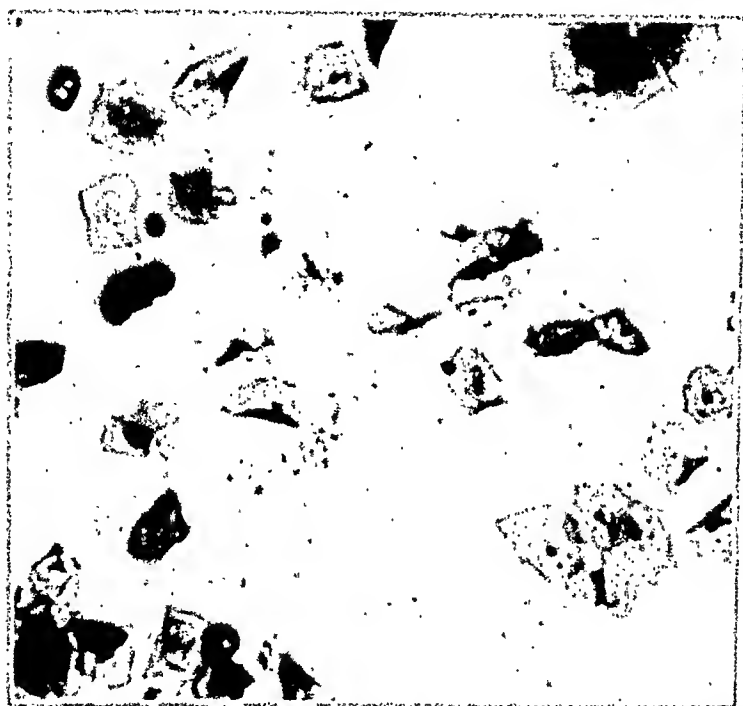


FIG. 10. (No. 5648.) Patient, aged twenty-five. Smear taken from nonpregnant woman after three other treatments for trichomoniasis. Absence of leucocytes, a few artifacts present. X245.

The microscopic picture is similar to that already described for other forms, with the exception that the epithelial and other layers have a somewhat different general appearance because of the histologic changes associated with the postmenopausal epoch. The leucocytic infiltration is of the same general type, and the inflammation produces similar alterations in and destruction of cellular elements (Fig. 11). At times bacterial invasion is marked in both the epithelial and sub-epithelial layers (Fig. 12). The reparative process appears to be similar in the latter two forms of vaginitis. That which takes place in the mycotic vaginitis has not been studied.

The restoration of the normal protective epithelial layer seems to be of paramount importance. M. E. Davis has reported the beneficial and

curative effect of hormonal therapy in cases of senile vaginitis while Lewis and others have had favorable results in the treatment of gonorrheal vaginitis in children by the administration of hormones. Both

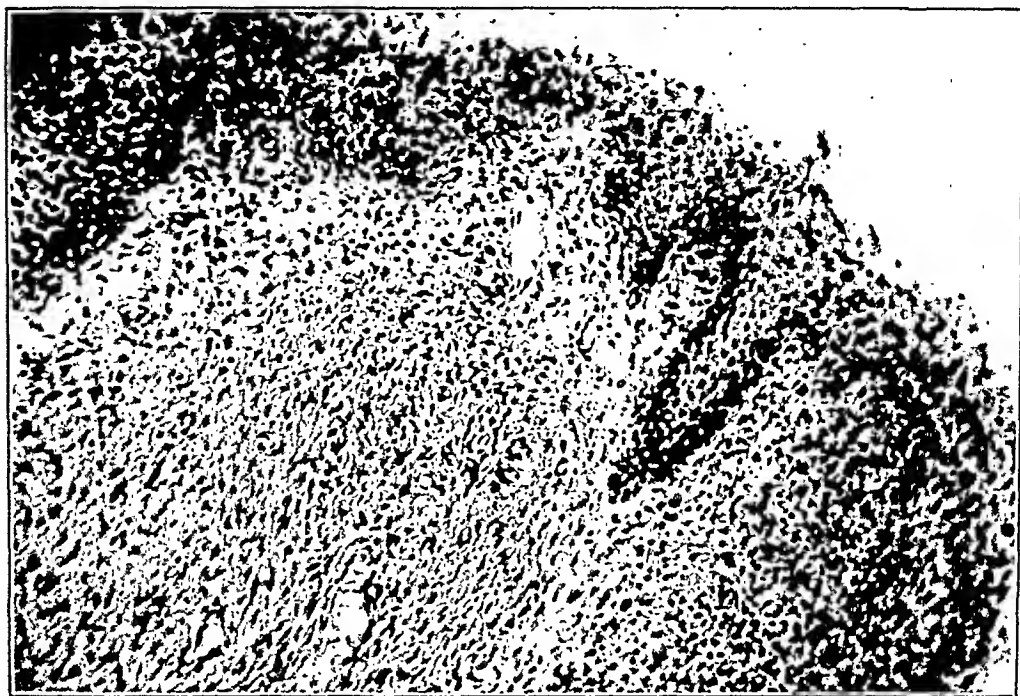


FIG. 11.—(No. 121888.) Patient, aged sixty-three. Biopsy taken from case of senile vaginitis before treatment. Destruction of epithelium and inflammatory reaction. $\times 210$.

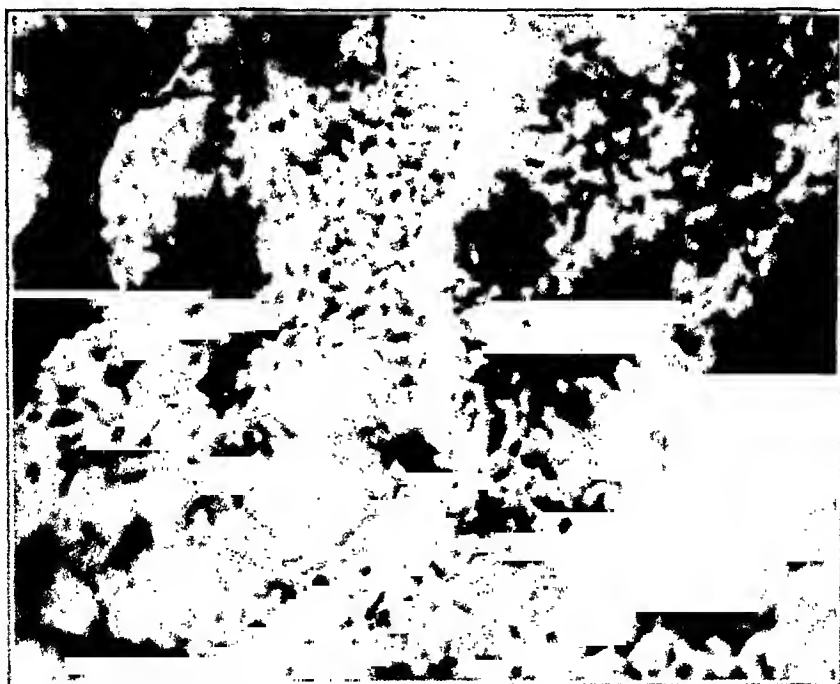


FIG. 17.—(No. 123415.) Patient, aged fifty-five. Biopsy taken from case of senile vaginitis before treatment. Bacterial invasion of subepithelial layer. $\times 2500$.

types seem to depend for their beneficial effects upon stimulation of epithelial growth (Figs. 13 and 14). We have attempted to show that



Fig. 13.—(No. 121887.) Patient, aged fifty-seven. Artificial menopause five years. Biopsy taken from area of trichomonads six weeks after institution of treatment. The small area of inflammatory infiltration. $\times 450$.

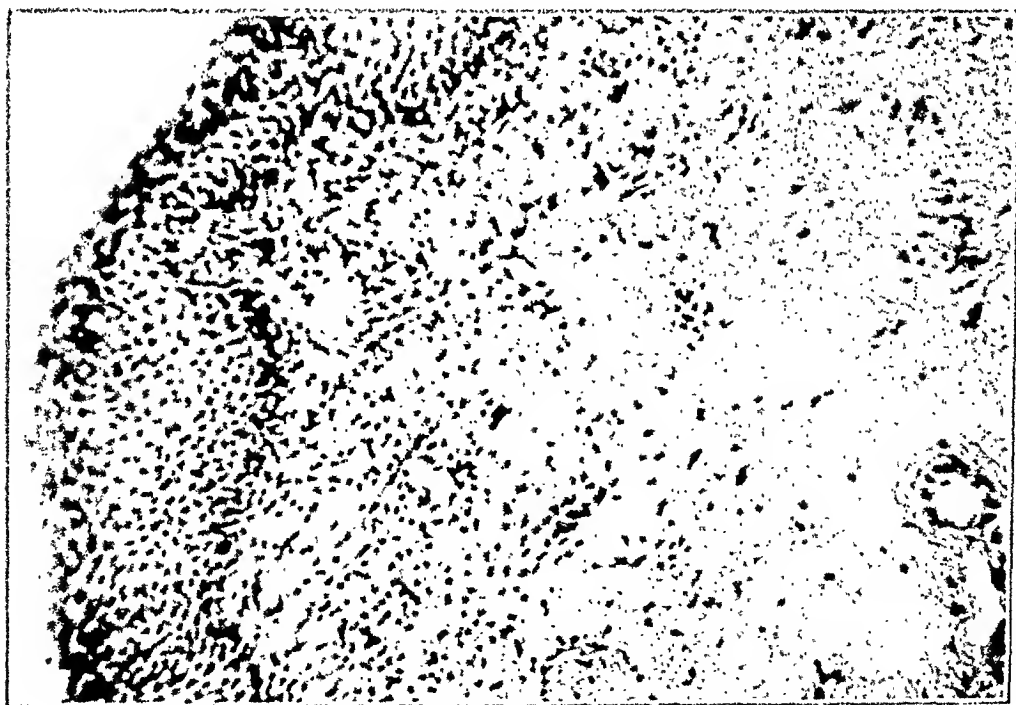


Fig. 14.—(No. 121888.) Patient, aged sixty-three. Biopsy taken from case of senile vaginitis six months after institution of treatment. Restoration of epithelial and sub-epithelial layers. $\times 215$.

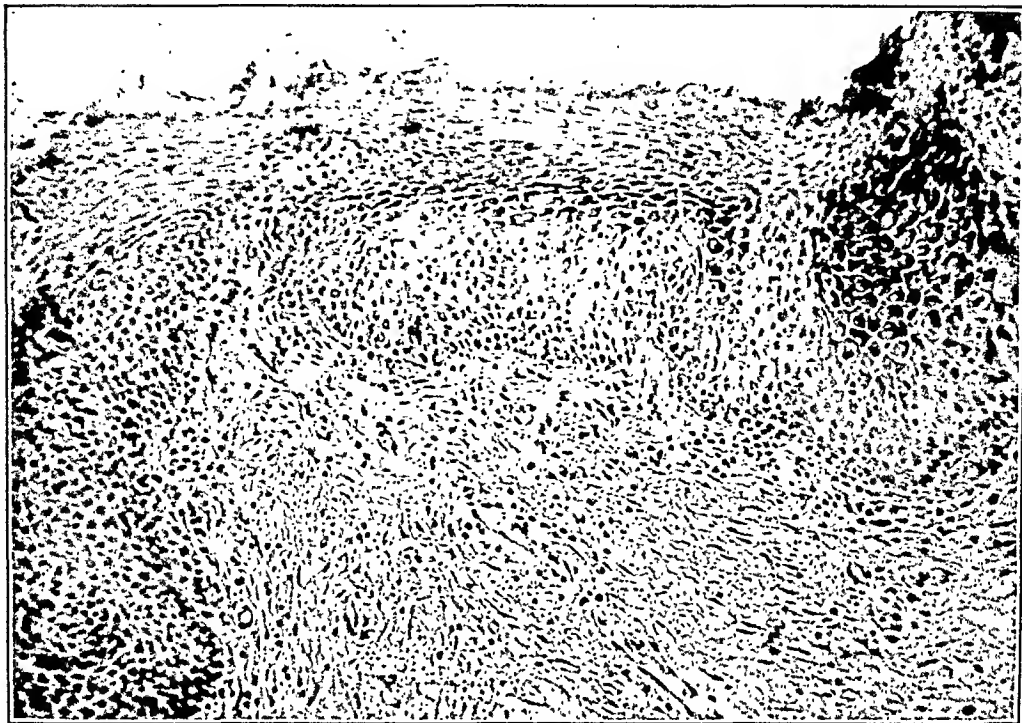


Fig. 15.—(No. 110285.) Patient, aged thirty-seven. Artificial menopause five years previously. Biopsy taken from case of trichomoniasis before treatment. Paucity of glycogen distribution. $\times 215$.



Fig. 16.—Same patient as in Fig. 15. Biopsy taken after institution of treatment. General distribution of glycogen, especially in the lower epithelial layers. $\times 215$.

the glycogenic content of the epithelium is an important factor in its restoration (Fig. 15), and we believe that the hormonal therapy may stimulate the production and deposition of glycogen in these tissues.

It is also our opinion that the artificial introduction of substances such as lactose into the vaginal canal may supply the vaginal flora with essential palatium, thus protecting the glycogenic content of the epithelial cells and furthering their normal growth (Fig. 16). It is also possible that the cells may absorb some of this material directly from the vaginal lumen. The presence of this chemical in the vagina also favors the growth of the vaginal bacillus which persists in a medium with a pH as low as 3.5.

The reparative process consists essentially in the restoration of a more nearly normal vaginal flora and pH with a gradual change in epithelial growth which results in a normal epithelial layer. The inflammatory reaction subsides and the leucocytes disappear.

A special study has been made of the glycogenic granules in these cells, and while some deposition is found in certain areas even during the period of active inflammation, these granules are much more abundant both in distribution and in intracellular deposition in normal health and during repair. It is of striking interest that the cells undergo considerable hypertrophy during this reparative process.

It is also noteworthy that the epithelial reactions, the cellular growth and the deposition of glycogen seem to be almost the same in cases of senile vaginitis treated by hormonal therapy and in those which have been treated by the intravaginal administration of lactose, 95 per cent, and citric acid, 5 per cent.

The therapeutic principle of creating conditions favoring normal tissue growth is, in our opinion, much more important biologically than any attempt to destroy pathogenic organisms by antiseptic or other agents.

PART II

BIOCHEMICAL APPROACH IN TREATMENT

Crickshank, Schröder, Curran and their respective coworkers have contributed and established considerable knowledge of the biology of the human vagina. The normal pH of the vaginal content ranges from 6.0 to 7.0 in childhood, 5.5 to 6.5 after the menopause, and 4.0 to 4.5 in the intermenstrual period. Menstrual and puerperal discharges alter the reaction temporarily. The acidity is caused primarily by lactic acid. A small amount of this acid may be liberated by the action of enzymes and by glycolysis of the carbohydrates, but the amounts found, especially during the childbearing period, are produced by the action of the vaginal bacilli upon the carbohydrate substance present in the vagina and vaginal walls. Hence, the degree of acidity is re-

lated directly to the bacterial flora and cellular content and certainly to the amount of nutritive (glycogen-like) material available. Oberst and Plass have made an excellent review of the literature on the acidity of the vagina.

The influence of antiseptics, foreign bodies, and chemicals upon the normal local metabolic process is unknown. Perhaps the destruction of the pathogenic bacteria by such means may also hinder the growth of the normal organisms. Whether there is any alteration of the local carbohydrate metabolism by such pharmacologic procedures remains to be established. From the foregoing it appears that injury to the epithelium alters the metabolic process, which becomes more abnormal as the insult increases. It is assumed that various types of bacteria may produce a vaginitis under certain conditions.

The pathogenicity of the vaginal trichomonads is still unsettled. However, the reports of Hibbert, Hesselstine, Allen, Jensen and Wood and others indicate that the bacteria associated with these flagellates are pathogenic, but the reports of Stein and Cope and others disagree.

The observations of Cleveland on the intestinal tritrichomonads and of Hesselstine and others on vaginal tetratrichomonads indicate that a particular type of bacterial flora is necessary for the existence of the protozoa, and that in the latter group these bacteria are abnormal for the vagina. Moreover, vaginal trichomonads are not found in the presence of a normal bacterial and cellular flora. The acidity of the vagina is distinctly less in this disease, usually varying from pH 5.0 to 6.5.

It is interesting, also, to recall that the normal acidity of the intermenstrual period is unfavorable for these flagellates.

Cornell,* Karnaky, and others have found that the husbands may reinfect and reinfest their wives, which agrees with our observations.

The specific etiologic agent of senile vaginitis is unknown, but inasmuch as the clinical entity is associated with an abnormal flora, bacteria are almost certainly the cause. The etiologic factors are not completely understood.

Yeastlike fungi (monilia and cryptococci) are established as pathologic agents in vaginal mycoses, and their prevalence in pregnancy and diabetes is striking (Hesselstine, Borts, and Plass). These organisms ferment glucose, levulose, maltose, and mannose regularly and often galactose and sucrose, but they do not ferment lactose. In the presence of yeast cells a mycosis may be produced or made worse by the use of glucose (Hesselstine). It will be shown later that lactose does not alter the course of a vaginal mycosis.

The above evidence indicates that if conditions favoring the growth of the vaginal bacilli and the production of a greater vaginal acidity

*Part of a communication.

are created, trichomoniasis, senile vaginitis, and perhaps some other infections may be treated successfully. The approach to the treatment of vaginal mycosis by another route seems best since this group of organisms behave differently and tolerate acidity well below pH 4.0 (Hesseltine and Noonan).

In bacterial infections the epithelial cells and their glycogen-like content need stimulation and perhaps protection. The substituting of a carbohydrate, which the vaginal bacillus can utilize and yet which does not favor the growth of a mycotic organism, is worthy of trial. Such a procedure will tend to correct a deficiency in the carbohydrate content in the vaginal epithelium and at the same time make conditions less favorable for growth of some of the pathogenic organisms.

Lactose was selected as it can be utilized directly by the vaginal bacillus, as shown by Lash and Kaplan and others, while glucose may be formed by the breaking down of the polysaccharides which might favor a mycosis. Although an attempt is made to increase the vaginal acidity by adding an acid, this may be unnecessary. Since liquids are not retained well in the vagina and since they tend to macerate the tissue, a dry preparation which might tend to dry the vaginal walls and to stimulate healing was desired. With the above prerequisites for a solid, relatively nontoxic acid, citric acid was chosen. This material is utilized by some bacteria.

The amount of citric acid was limited to 5 per cent, since it was believed that as solution gradually took place there would be sufficient acid to affect trichomonads and abnormal bacteria unfavorably and yet not damage the vaginal bacilli. It was hoped that ranges of pH from 4.0 to 4.5 would continue for several hours.

TREATMENT

A mixture of lactose (95 per cent) and citric acid (5 per cent) is used for office treatment. Tablets of 2 gm. amounts for daily home treatment were made from a preparation containing one pound of starch paste to one gallon of this mixture.

The patient has one to two heaping teaspoonfuls (3 to 6 gm.) of lactose (95 per cent) and citric acid (5 per cent) placed in the vagina after the diagnosis of trichomoniasis or senile vaginitis is established. The patient is instructed to place two 2 gm. pills of this material in the vagina each evening upon retiring. Usually the patient is instructed to return in one week for reexamination and thereafter the intervals vary from two to three weeks, depending upon the response to treatment. Infections of the cervix and other sites are treated by appropriate means simultaneously with the carbohydrate therapy, and in these instances more frequent visits to the clinic may be necessary. The patients are instructed to use no douches. Occasionally the ma-

terial tends to accumulate as the condition improves, and in these instances a plain water douche may infrequently be employed. During menstruation all treatment is discontinued. Sexual abstinence is urged particularly during the acute stage, but when it is indulged in, condoms are recommended to avoid spreading the disease as well as to obviate reinfection.

RESULTS

To evaluate the action of glucose and of lactose applied in the vagina, 25 controls were used (see Table I). Glucose and citric acid were used four times in the absence of fungi in normal healthy patients without symptoms or macroscopic tissue changes developing. Glucose and citric acid produced or made a vaginal mycosis worse in five patients with fungi. The lactose was used in four normal, healthy patients without fungi, and in twelve with fungi, and in both groups there were no subjective or objective changes.

TABLE I. CONTROLS OF CARBOHYDRATE THERAPY IN VAGINAL TRICHOMONIASIS AND OTHER INFECTIONS

	IN ABSENCE OF FUNGI	IN PRESENCE OF FUNGI
Glucose with citric acid	4—Unchanged	5—Mycosis developed or made worse
Lactose with citric acid	4—Unchanged	12—Unchanged

During the period of study there have been 112 consecutive cases of vaginal trichomoniasis and 5 of senile vaginitis. Of the 112 (Table II) 35 were discarded as 28 did not return after the initial visit and 7 were given mixed treatments through a misunderstanding. Obviously, the good or bad results could not be accredited to any one procedure. This leaves 77 trichomoniasis cases for study. Of this number 12 women were pregnant and 65 not pregnant. "Cured" indicates that the patient has passed through two menstrual periods without a recurrence of symptoms and that there is no evidence of the disease on clinical appearance or smear study. "Improved" means that the patient is under treatment and observation with distinct improvement, or that the patient was benefited objectively and subjectively on her last visit but has discontinued clinic visits.

TABLE II. RESULTS OF CARBOHYDRATE THERAPY IN 117 CONSECUTIVE ADULT CASES (112 TRICHOMONIASIS—5 SENILE VAGINITIS)

	TRICHOMONIASIS	SENILE VAGINITIS	TOTAL
Untreated	28	0	28
Treatment interrupted	7	0	7
Improved	39	3	42
Cured	38	2	40
			117

To date (Table III) 5 pregnant and 32 nonpregnant women have been "cured" of trichomoniasis while 7 and 33, respectively, have been improved. In the scabic vaginitis group 2 have been "cured" and 3 "improved."

TABLE III. Duration and Frequency of Treatment

	TREATMENT WITH OTHER AGENTS				NUMBER OF TREATMENTS		MONTHS OF TREATMENT		NUMBER OF RECURRENCES	
	HYPOPHOSPHITES	HYPERMANGANATE	HYPERMANGANATE	HYPERMANGANATE	HYPOPHOSPHITES	HYPERMANGANATE	HYPOPHOSPHITES	HYPERMANGANATE	HYPOPHOSPHITES	HYPERMANGANATE
Trichomoniasis										
Pregnant										
Improved	1	0	0	0	1	0	1	0	1	0
Cured	4	1	1	1	5	3	5	3	5	3
Nonpregnant										
Improved	2	0	0	0	2	0	2	0	2	0
Cured	30	3	3	3	33	6	33	6	33	6
Scabic vaginitis										
Improved	0	0	0	0	0	0	0	0	0	0
Cured	1	1	1	1	2	2	2	2	2	2

*Occurred postpartum.

*Three husbands positive test of infection and reinfection.

Four husbands possible test of reinfection and reinfestation.

There was one recurrence which occurred postpartum in the obstetric group. Seven of the 32 cured cases had recurrences. In three instances husbands were found to have trichomonads in the prostatic secretion. In four it is possible that the husbands may have had an infection and infestation for in each there is a history of recurrence shortly after coitus. In the 3 known cases of prostatic trichomoniasis the recurrences came on a few days following copulation. Because of potential contagion these infected and infested males should receive urologic treatment.

It will be noted in Table III that the periods of treatment are rather long. This is due in some instances to poor cooperation on the part of the patient and in others to the fact that severe or extremely chronic cases had been under various other treatments for many months without cures before receiving this treatment. Some patients responded slowly while others responded very rapidly. The photomicrographs illustrate the extreme degree of inflammation that occurs at times in the epithelial and subepithelial layers. Furthermore, prompt and immediate cures are uncommon. An attempt has been made to follow our patients over as long a period as is feasible in order to evaluate the results of this treatment properly, but this has been difficult because many patients are satisfied if pain, tenderness, and local irritation are removed.

In the acute stage the lactose and citric acid preparation may cause some irritation or burning which disappears as the condition improves. Usually the patients have not objected to this reaction. In the warmer months, three patients had vulval irritation which seemed to be associated with the perspiration and the discharge in producing some maceration of the tissue. This cleared up very promptly after a few days' rest from treatment and did not recur on reinstitution of the therapy. These pills usually cause a slight watery discharge which may appear shortly after insertion or on the following morning when the patient arises. This reaction has been associated with a good response to treatment. The tablets should be made up free of materials which are fermented by the monilia. The tablets as they are compounded are nonpoisonous and inexpensive.

It is planned later to study the value of citric acid and investigate the action of some other carbohydrates. Those carbohydrates which are fermented by the monilia and the cryptococci will almost certainly be eliminated. Those disaccharides and polysaccharides which liberate glucose molecules as they are broken down by enzymes may be eliminated also.

SUMMARY

1. Vaginal trichomoniasis and senile vaginitis have been cured by using lactose (95 per cent) and citric acid (5 per cent) therapy. Focal infections have been treated simultaneously by appropriate means. Although recurrences have developed there have, as yet, been no failures.

2. Generally, vaginal trichomoniasis and senile vaginitis respond slowly to treatment. The maximum period of treatment and observation was ten months in one instance, while the minimum was two months.

3. The average number of clinic visits in the "cured" group was 6.2, 9.2, and 8.3 for the pregnant trichomoniasis, nonpregnant trichomoniasis, and senile vaginitis patients, respectively. The respective average time intervals for treatment and observation were 2.7, 4.4, and 4.5 months. Perhaps these averages are higher than are necessary, especially since several of these were severe and extremely chronic cases which had not responded to other procedures.

4. Some recurrence of vaginal trichomoniasis and probably some exacerbations are due to reinfection and reinfestation from sexual partners.

5. The principle of this therapy is to supply directly nutritive substances which are necessary for a normal vaginal flora. This nutritive material may be supplied indirectly as a result of hormonal stimulation after the menopause.

DISCUSSION

DR. EDWARD ALLEN, CHICAGO, ILL.—These studies should be extended to include all those organs intimately associated with the infected vagina. I would include in this list, the urinary system, bartholinian glands, the cervix, uterus, and fallopian tubes, adding also the bladder, urethra, and prostate in the male.

We have found a rather typical picture in twenty-eight of forty lower female urinary systems studied through the urethroscope or cystoscope. The pathologic changes in the mucous membrane of these organs suggest an actual invasion either by tissue continuity or ascending infection.

We have isolated similar strains of streptococci from the prostate in the male and the bartholinian gland in the female as those found in the infected vaginal secretions. These streptococci seem to be of the arthrotropic variety as determined by electrical potential, and many of the aches and pains elsewhere in the body might be explained by their presence.

The high incidence of increased blood loss in these patients suggests that extension to the upper müllerian tract is entirely possible. I am beginning to believe that many of the otherwise unexplainable pelvic infections and postoperative complications have their origin in this manner.

The percentage of permanent cures reported by Dr. Hesseltine are about the same as those reported by other investigators. It has been my feeling that, since most of us can cure approximately 80 per cent of patients whom we treat, that if we could discover the methods of re-infection, prophylaxis and permanent cure would be relatively simple. I am convinced that transfer of the guilty organism from the female to the male and back again will explain many of these recurrences. We have found the *trichomonas vaginalis* in prostatic secretion of many of our male patients and in many more of them a coccus prostaticitis.

DR. RALPH A. REIS, CHICAGO, ILL.—There is one problem I want to bring up, namely the rather great frequency with which we find trichomonas in patients who have or have had gonorrhea. We have had twelve or more patients in whom trichomonas infection developed while we were treating them for gonorrhea, and in seven or eight of them we were able to demonstrate the gonococcus at the same time that we found the trichomonas. The usual experience is that the gonococcus disappears when the trichomonas becomes rampant.

I can understand the etiology of the trichomonad infestation, where there is some type of infection in the male, but I would like someone to offer some explanation of the sudden appearance of this type of vaginitis in virgins.

DR. J. C. LITZENBERG, MINNEAPOLIS, MINN.—I have been impressed by the ease with which these patients can be improved by most methods of treatment, but they are as bad as ever after menstruation. Since I have continued treatment during menstruation my results have been better. Whether this particular treatment outlined by the essayists will lend itself to treatment during menstruation I do not know.

DR. JAMES R. MANLEY, DULUTH, MINN.—What did you say about using a pound of starch to a gallon of water?

DR. JEAN PAUL PRATT, DETROIT, MICH.—Some years ago we tried taking a piece of the vaginal wall when a complete hysterectomy was done in the hope of finding some cyclic change. We were unable to draw any conclusions.

Dr. Hartman has found that by combining resorcin and tannic acid he has raised the bacteriologic coefficient very high without increasing the toxicity. The com-

THE HYDROGEN ION CONCENTRATION OF HUMAN VAGINAL DISCHARGE*

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IT IS generally accepted that the normal vaginal discharge is acid in reaction, but relatively little attention has been given to its hydrogen ion concentration and to determining the alterations which may be developed in the individual by physiologic changes and by disease. This study is concerned chiefly with the development of a simple method for the electrometric determination of the pH of the undiluted discharge and its relation to the vaginal flora. Since the entire subject has received practically no mention in American medical literature, an attempt has also been made to review critically the more significant work from European, especially German, sources.

HISTORICAL REVIEW

Although it had been demonstrated by Zweifel,¹ in 1877, that the vaginal discharge is commonly acid in reaction, study of the problem was stimulated by Döderlein,² who noted that the acidity was reduced in certain pathologic conditions involving infection (more commonly in parous women with clinical abnormalities, such as cervical erosions, cervicitis, condylomas, and granular vaginitis), and related the degree of acidity to the presence of certain large, gram-positive bacilli, which are now recognized as the "vaginal bacilli of Döderlein." He also determined that the acidity is due largely to lactic acid, a direct product of the activity of the vaginal bacilli, and attempted to estimate its concentration by titration. Shortly thereafter Menge³ demonstrated that the acidity of the normal discharge is sufficient to kill streptococci in from two and one-half to seventy hours, and therefrom developed the conception that the acid reaction offers an element of protection, especially during menstruation and parturition. Hinrichs⁴ later confirmed these findings by showing that the vaginal bacilli will kill off other organisms in a few days. The vaginal bacilli can grow at a pH as low as 3.6 to 3.9, whereas other vaginal organisms are killed at pH 4.5 within one or two days and their tolerance lies at about pH 5.0 to 5.5.

Stroganoff⁵ showed that the vagina contains bacteria throughout life and that the acidity varies with the flora, being high during sexual maturity and especially during pregnancy, when the vaginal bacilli are most numerous. Perle⁶ developed the idea that there is a reduced acidity or even an alkalinity for two days before, during, and for two days after menstruation, and claimed that in the course of amenorrhea, due to chlorosis, anemia, or lactation, the discharge becomes alkaline during the two or three days each month which correspond to the missed menses. He also noted variations during pregnancy, the reaction becoming less acid during the second trimester, stronger again as term is approached, and alkaline during the early puerperium.

Zweifel¹ in 1908, demonstrated that the acidity is due to racemic lactic acid and differentiated between its "bound" and "free" forms, both of which are present

*Presented in preliminary form before the American Chemical Society, Chicago, September, 1927. Released for publication, December, 1927.

in diminished concentration in pathologic secretions. He also showed that the vaginal bacilli can utilize glycogen but not glucose.

In this country, Williams⁸ confirmed many of these findings, and was in great part responsible for the development of this branch of bacteriology, and for spreading the doctrine that the character of the vaginal discharge during pregnancy in normal women offers such effective protection during labor that antepartum douches are harmful rather than beneficial.

Gräfenberg,⁹ in 1918, reopened the discussion, stressing his belief that it is possible to demonstrate rhythmic variations in the vaginal acidity during the menstrual cycle, and that such changes are independent of actual menstrual bleeding, since they were observed in the course of normal pregnancy, as well as in a woman after hysterectomy. It was his contention that the acidity of the vagina diminishes from shortly after the cessation of the flow to the middle of the intermenstrual period, when there is an interval of reduced acidity related to the rupture of the follicle, and then rises to its highest point shortly before the next period. The lowered acidity during the midmenstrual interval ensures optimum conditions for the spermatozoa and produces the most fertile period during the cycle. Since these cyclic changes disappear after the menopause, they are related to ovarian function. Heinlein,¹⁰ using Gräfenberg's technique, was unable to detect regular cyclic changes in acidity but did note slight variations from day to day.

Heurlin¹¹ called attention to the relation between the bacterial flora and the acidity of the vagina, and offered a classification, which was later revised by Loesert¹² and by Schröder,¹³ whose simple grouping, which has been widely adopted in Europe, is as follows:

Type I contains only gram-positive vaginal bacilli,

Type II contains, in addition to the vaginal bacilli, cocci-bacilli, diplococci, variable comma, anaerobic streptococci, and various other organisms, and,

Type III contains no gram-positive vaginal bacilli, with disappearance of the variable comma and predominance of cocci of all varieties.

Schröder¹³ noted the following distribution in the 288 nonpregnant women studied:

Type I	113 cases	39 per cent
Type II	55 cases	19 per cent
Type III	120 cases	42 per cent

The reaction of the discharge in Type I was invariably acid, while in Type II it was alkaline only in two patients, who had copious mucous cervical secretions. On the other hand, Type III discharges were amphoteric in 22 and alkaline in 11 cases.

Schultheiss¹⁴ attempted to correlate the type of vaginal flora in nonpregnant individuals with the hydrogen ion concentration determined on centrifuged vaginal washings by the Michaelis colorimetric method with the following results:

TYPE OF DISCHARGE	NO. OF CASES	HYDROGEN ION AVERAGE	CONCENTRATION RANGE
I	77	4.7	3.92-6.85
II	83	5.57	4.25-7.62
III	172	6.2	4.72-7.62

Günssle¹⁵ had previously recorded similar observations in the nonpregnant and had shown that during gestation the various types of discharge are associated with similar hydrogen ion concentrations, as follows:

TYPE OF DISCHARGE	NO. OF CASES	HYDROGEN ION AVERAGE	CONCENTRATION RANGE
I	20	4.5	3.95-4.85
II	6	5.1	5.1 -5.6
III	34	6.03	5.3 -6.7

The proportion of Type I discharge is greater during pregnancy (compare previous tables), a fact which was noted also by Lehmann,¹⁶ who found the vaginal bacilli alone in only six among 600 gynecologic patients, but recorded Type I discharge in 82 per cent of women four to five months pregnant and in 51 per cent of those in the last month of gestation. On the other hand, Cruickshank and Sharman¹⁷ noted that the incidence of Type I discharge increases as term is approached and that in individual patients a Type II or Type III discharge may be replaced spontaneously by Type I in the latter months of pregnancy. In contrast to Lehmann,¹⁶ these investigators found 44 per cent Type I in the first, 57 per cent in the second, and 64 per cent in the third trimester of pregnancy, among 83 patients examined repeatedly during gestation.

Since Döderlein² offered his evidence that the vaginal acidity is due largely to the action of the vaginal bacilli in producing lactic acid, considerable attention has been directed at this phase of the problem. Zweifel⁷ believed that the bacteria act upon glycogen but not upon glucose, a view which is favored by Loeser,¹² Lehmann,¹⁶ Cruickshank and Sharman,¹⁸ Geller,¹⁹ and Menge.²⁰ On the other hand, Demme and Baltzer²¹ showed that the glucose content tends to be high when the pH is low, results which contradict Kessler and Uhr,²² who found that the sugar content of the vaginal secretion is lower and the glycogen content higher with Type I discharge. Demme²³ reported that both the glycogen and the glucose are diminished when the acidity is reduced and a Type III discharge appears during menstruation. Kessler²⁴ found the vaginal discharge alkaline during the first week after delivery, but noted that it becomes slightly acid during the second week, when the quantity of glucose increases even though glycogen cannot be demonstrated. Von Jaschke²⁵ insists that the glycogen of the vaginal epithelium does not parallel the lactic acid content, and believes that the acidity may be due in part to acids other than lactic.

Hubert²⁶ was able to grow the vaginal bacilli in pure culture in glucose-containing media, which uniformly developed an end pH of 4.0 to 4.1, irrespective of the quantity and concentration of the media, or of the extent of the original inoculation. In glucose-free, glycogen-containing media, a few strains of vaginal bacilli gave luxuriant growths. It has been suggested by Gragert,²⁷ and others, that the vaginal mucosa may contain a diastatic ferment which changes glycogen to glucose, which is then acted upon by the vaginal bacilli. Schröder, Hinrichs, and Kessler²⁸ likewise believe that the vaginal bacilli cannot utilize glycogen directly and incline to the idea of an intermediary ferment. Hubert,²⁶ however, concluded that the production of acid in glucose-free, glycogen-containing media must result directly from bacterial action without the intervention of a ferment. Schultheiss²⁹ supported this contention when he showed that while the vaginal bacilli can produce lactic acid in glycogen media, a bacteria-free vaginal discharge thinned with normal salt solution cannot develop lactic acid in the same medium.

Loeser¹² and Lehmann¹⁶ express the belief that the glycogen content of the vaginal epithelium is related in some fashion to ovarian activity. Cruickshank and Sharman¹⁸ determined the glycogen content of the vaginal mucosa at various age periods and decided that the deposition of glycogen in this structure is dependent upon the presence of estrogenic hormone in the circulation. The observed pH and the vaginal flora were influenced by the glycogen content of the vaginal mucosa, which in turn varied directly with the output of estrogenic substance through the urine. Vaginal bacilli and a low pH are associated during the first month of life, while the hormone which has been transmitted to the fetus from the mother by way of the placental circulation is still present and active, and during the period of sexual activity from puberty to the menopause, while opposite conditions prevail during childhood (from

the age of one month to puberty) and after the menopause. Dierks,³⁰ after histologic examination of the vaginal mucosa excised from a series of normal women, concluded that this structure undergoes regular changes during the menstrual cycle. Davis and Hartman³¹ have described comparable cyclic variations in adult female rhesus monkeys and have presented a comprehensive summary of the controversy which followed Dierk's publication.

Engelhorn³² concluded that the bactericidal effect of the vaginal discharge depends essentially upon its acid content, since it increases considerably in old cultures the acidity of which has been augmented by long standing in the incubator. This argument had been advanced previously by Zweifel,⁷ who for this reason recommended antepartum douches of lactic acid to increase the bactericidal action of the vaginal discharge. When the vagina becomes infected with organisms other than the vaginal bacilli (discharge of Type II or III), the acidity is commonly reduced. Loeser³³ believes that this change toward alkalinity may be due to inflammatory reactions in the vaginal epithelial cells interfering with the secretion or deposition of glycogen. It is, however, generally recognized that an increased amount of cervical secretion, which is distinctly alkaline, may disturb the vaginal acidity, and tend further to reduce the determinable acidity. Lehmann¹⁶ thinks it very improbable that a lack of vaginal bacilli is the primary cause of the reduction of acidity in patients with pathologic discharges. It may be that these organisms die off because they do not obtain sufficient nourishment (glycogen or glucose) through the inflamed vaginal mucosa. Loeser³³ has advanced the conception that the vegetative nervous system controls the lactic acid production, while others feel that the general condition of the woman determines the amount of available glycogen and, therefore, the formation and the amount of lactic acid.

DISCUSSION OF THE METHODS USED FOR THE DETERMINATION OF THE VAGINAL ACIDITY

The earlier investigators used litmus paper to determine vaginal acidity. Menge³ heated the paper after exposure to demonstrate that the acidity is due to a free non-volatile acid or to acid salts rather than to dissolved carbon dioxide. Gänssle¹⁵ pointed out that red litmus paper turns blue at a pH of 6.6, which explains the statements of earlier authors that the vaginal discharge is not infrequently alkaline in reaction.

Döderlein³⁴ determined the acidity in terms of lactic acid equivalents by titration and found an average value of 0.945 per cent for the normal vaginal discharge. Zweifel⁷ found a maximum lactic acid content about one-half that reported by Döderlein, with a range of from 0.3 to 0.5 per cent.

Gräfenberg,⁹ Heinlein,¹⁰ and others, washed the vagina with measured quantities of neutral distilled water or normal saline solution and titrated the filtered or centrifuged washings against 0.01 or 0.02 N NaOH, using phenolphthalein as the indicator. Results were expressed in terms of the amount of standard alkali necessary to effect neutralization. It is obvious that the total acidity varies with the amount of the discharge, a fact which serves to explain certain differences between their findings and those obtained by more modern methods. Moreover, titration determines both the bound and the free acid.

Kraul and Bodnar,³⁵ in 1925, introduced a microtitration method based upon the use of undiluted discharge which is subject to certain of the same criticisms. They measured 0.5 to 1.0 c.c. of discharge, titrated it against 0.01 per cent NaOH, and calculated the percentage of acid.

With the realization that the action of an acid solution depends more upon the proportion of hydrogen ions than upon the total amount of titratable acid, attention

was turned to the hydrogen ion concentration of the discharge. In certain instances (Schultheiss,¹¹ Glüssle,¹⁵ and Gragert²⁷), the vagina was washed as in the earlier work and the pH determined colorimetrically, while others (Behrens and Naujoks³⁶) used an electrometric method. Abraham³⁷ pointed out the fallacies inherent in any method that requires dilution with unbuffered solutions. Behrens and Naujoks³⁶ had, however, reported that dilution up to 100 times with physiologic salt solution does not affect the pH as determined electrometrically, since for practical purposes the vaginal discharge is a well-buffered solution, but record only one experiment to support this contention.

The undiluted discharge has been employed by Kessler and Uhr²² and by Demme and Baltzer²¹ for the electrometric determination of the hydrogen ion concentration, while Cruickshank and Sharman¹⁷ apparently employed a microcolorimetric method using standard indicators.

CONCLUSIONS FROM THE LITERATURE

Results obtained by the various workers have been divergent, but certain conclusions seem justified. More work under carefully controlled conditions using the best methods of attack is required before the picture can be completed.

In newborn children there are certain changes in the vaginal acidity which are stressed particularly by Cruickshank and Sharman,¹⁷ whose observations confirm those of Abraham,³⁷ and Gragert.²⁷ At birth the vagina is acid but sterile, the acidity apparently varying with the amount of contamination with amniotic fluid. Kienlin³⁸ has shown that this acidity is due to lactic acid, which he believes to come from glycogen through the action of an enzyme. Within two or three days, vaginal bacilli make their appearance and the acidity rapidly increases to pH 4.0 to 5.0 with a moderately profuse discharge. During the second week, the discharge is scanty but still markedly acid. At the end of the first month, the secretion is small in amount and tends to be considerably more alkaline, usually in the neighborhood of pH 7.0, although it may be as low as pH 5.0. During the remainder of childhood up to puberty, the discharge is commonly neutral or alkaline. After the first growth of vaginal bacilli, during the early days of life, these organisms disappear more or less completely and rapidly and a mixed flora develops.

Cruickshank and Sharman¹⁷ relate these changes to the action of the estrogenic hormone, which presumably controls the deposition of glycogen in the mucosa of the vagina and thus determines the vaginal flora. They found that in fetuses and newborn infants up to five days after birth there is abundant glycogen in the vaginal mucosa. After this period, the glycogen becomes less abundant until, from the age of one month to puberty, it is absent. Corresponding changes occur in the histologic picture of the mucosa, which is "many-layered and florid" at birth and for a few days thereafter, but which rapidly becomes atrophic and thinner until from the age of one month to puberty it is composed of only a few layers of epithelial cells. It is their conception that the fetus obtains so much estrogenic hormone through the placenta from the mother's blood that the vaginal mucosa takes on an adult appearance during the latter months of intrauterine life, but that birth eliminates this source of supply, and the mucosa quickly atrophies, to be restimulated only when follicular development begins in the ovaries shortly preceding the first menstruation. These observations are in accord with those of Lewis,³⁹ who recently recorded his experiences with changes in the vaginal mucosa following the injection of diethyl-steroids into children, and who has developed the plan of treating vaginal infections, especially gonorrheal vulvovaginitis, in children by encouraging the growth of an

adult-type mucosa, which is more resistant to infection. It is well recognized that children during the first month of life do not contract gonorrheal vaginitis, whereas from then until puberty they are particularly susceptible to this form of infection.

From the time of puberty to the menopause, it is generally agreed that the vaginal discharge is normally decidedly acid and that the sole or predominating organisms are the vaginal bacilli. { The mucosa is of the adult type with many layers of epithelium which contains abundant glycogen. As shown by Soeken,⁴⁰ this change from childhood to adult conditions is very abrupt, occurring within one to two weeks. The pH in sexually mature women is normally between 4.0 and 5.0, with the average at or below 4.5. Infection from without alters the situation, leading to a mixed flora (Types II and III) and to a diminished acidity, with the reaction, however, rarely if ever reaching neutrality. Eradication of the infection leads to the return of a normally acid discharge.

The balance of opinion favors slight, more or less rhythmic, alterations in the vaginal acidity during the menstrual cycle, the most generally found change being a slightly increased acidity in the premenstrual period (Guthmann and Koch⁴¹), which is related by Geller,⁴² and others, to an increased glycogen content of the vaginal mucosa induced by the augmented production of estrogenic hormone in the ovary. It seems that the reaction does not become alkaline even during the period of bleeding, provided precautions are taken to exclude the alkaline blood and cervical secretion from the sample.

During pregnancy, in women with a normal flora, there is an increased amount of discharge due to the marked hyperemia, but probably little, if any, change in the acidity. The amount of glycogen in the mucosa is increased, a condition which apparently encourages the growth of the vaginal bacilli, so that there is frequently a spontaneous change in the flora from Type II or III to Type I and an associated increase in the acidity to normal limits. Individuals who begin pregnancy with Type I discharge and high acidity tend to maintain these conditions until delivery, the acidity effectively preventing the establishment of introduced organisms.

Within a few days after delivery, the vaginal flora becomes mixed, the presence of the bloody lochia apparently encouraging this change by making the discharge more alkaline, and therefore is better suited to the growth of other organisms. Within three or four weeks, the vaginal bacilli are again well established and the reaction becomes normally acid. Kessler.⁴²

After the menopause, there is a decrease in acidity associated presumably with the disappearance of the estrogenic hormone from the blood due to gradual atrophy of the ovaries, and apparently comparable to the more abrupt changes induced by birth. The same alterations occur, but more rapidly, in the surgical menopause produced by complete oöphorectomy. In either instance, the vagina becomes more susceptible to infection and a mixed flora becomes the rule. The glycogen disappears from the epithelial cells, and, in general, conditions are similar to those obtaining in childhood.

EXPERIMENTAL DATA

The New Microelectrode.—A quinhydrone microelectrode (Fig. 1) was designed to permit the electrometric determination of the pH of a small amount of vaginal discharge collected directly from the vaginal wall without dilution or contamination. The upper end of the platinum point of the plunger (shaded) was fused to the copper wire above the glass-platinum union, while the lower 1.0 cm. portion lay free in a small (1.0 mm.) capillary glass tube. The amount of dry quinhydrone that would adhere to the exposed clean platinum wire was used to saturate the material under investigation, which was drawn directly into the capillary tube by mouth suction through the side arm of the assembled apparatus. After an interval (five minutes) allowed for saturation of the fluid with quinhydrone, the copper lead was connected with a calomel cell and the difference in potential (in millivolts) read from a standard potentiometer. The pH was obtained from a prepared graph by subtracting a correction factor of 0.01 pH for each degree of room temperature below 38° C.

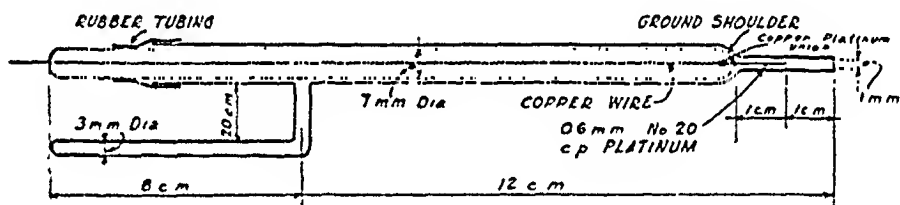


Fig. 1.

METHOD OF OBTAINING MATERIAL

The vaginal mucosa was exposed with a dry sterile bivalve speculum, and the discharge was drawn directly into the electrode tip by suction. In each experiment two electrodes were filled, one from the lateral wall just inside the hymeneal ring (anterior or lower) and the other from the lateral fornix near the cervix (posterior or upper). Smears taken from the same locations were stained by Gram's method. For determining the effect of dilution, 15 c.c. of neutral distilled water were introduced into the vagina and agitated before a sample was removed for analysis.

RESULTS

General Data.—Among the 177 determinations which are reported, the pH range was from 3.86 (normal nonpregnant) to 7.69 (nonpregnant menstruating, with pathologic discharge). Although our interest was not particularly in the vaginal flora, the stained smears were graded according to Schröder's¹² criteria. Close correlation was observed between the type and number of microorganisms and the acidity, which was high in the presence of large numbers of the vaginal bacilli and low in their absence. Occasionally, there was a relatively high acidity in the absence of the usual long Döderlein bacilli, but in

such cases short gram-positive rods or cocci-bacilli were present in abundance and were looked upon as unusual forms of the same organism. The vaginal bacilli were usually absent when gonococci were present but returned as the disease responded to treatment. The vaginal acidity was reduced in both nonpregnant and pregnant women with gonorrhea.

Fig. 2 shows the frequency distribution of the hydrogen ion concentrations in the lower pH groups in nonpregnant and pregnant women with normal and pathologic vaginal floras, and demonstrates graphically the diminished acidity in patients with discharges of Types II and III.

Nonpregnant Women With Normal Discharge (Type I).—It was difficult to find nonpregnant women who had bacteriologically normal discharges and who would cooperate. Consequently, only seventeen observations are recorded on two individuals

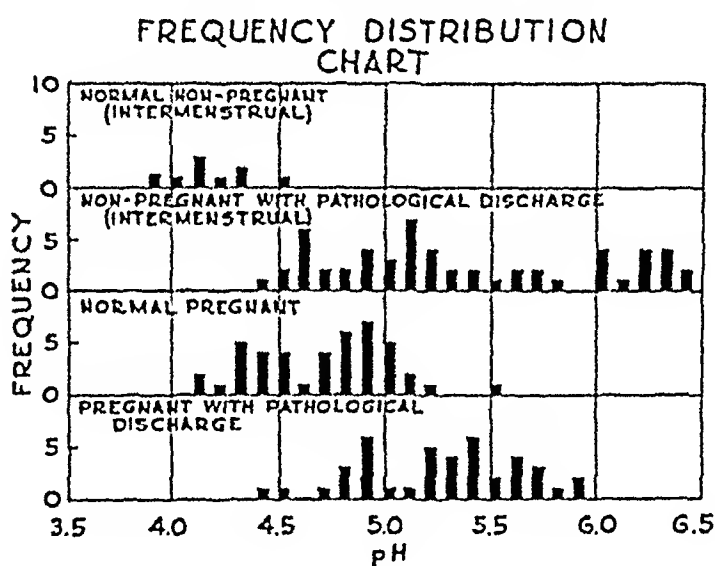


FIG. 2.

(Table 1). During the intermenstrual period, the pH was consistently low, 3.86 to 4.59, and the average values for the upper and lower vagina showed no variation. In each instance the cervix was normal and there was no clinical leucorrhea. During menstruation, the readings were almost invariably higher than during the interval even though every care was taken to exclude blood, and in two instances the discharge was actually alkaline (pH 7.07 and 7.15) on the third and second days of the flow.

Nonpregnant Women With Pathologic Discharge (Types II and III).—Fifty-six observations are recorded (Table II) during the intermenstrual period with only a few readings lower than pH 4.59, the maximum observed in the normal group. Moreover, in every individual the average pH was above this level. The average acidity of the upper vagina was less than that of the lower portion of the tract. These patients had cervicitis with profuse cervical discharge and clinical leucorrhea, and it is believed that this condition explains the reduced acidity in the upper vagina. During menstruation there was a further increase in the average pH with the upper vagina giving readings near the neutral point. In each individual, the specimen from the upper vagina was above pH 7.0 at some time during the flow.

Cyclic Variations During Menstruation.—Fig. 3 shows graphically the variations in vaginal pH during a lunar month in women with normal and abnormal floras, while Fig. 4 (upper portion) represents a smoothed curve from the same data. On the other hand, Fig. 4 (lower portion) is a smoothed curve from data on total acidity

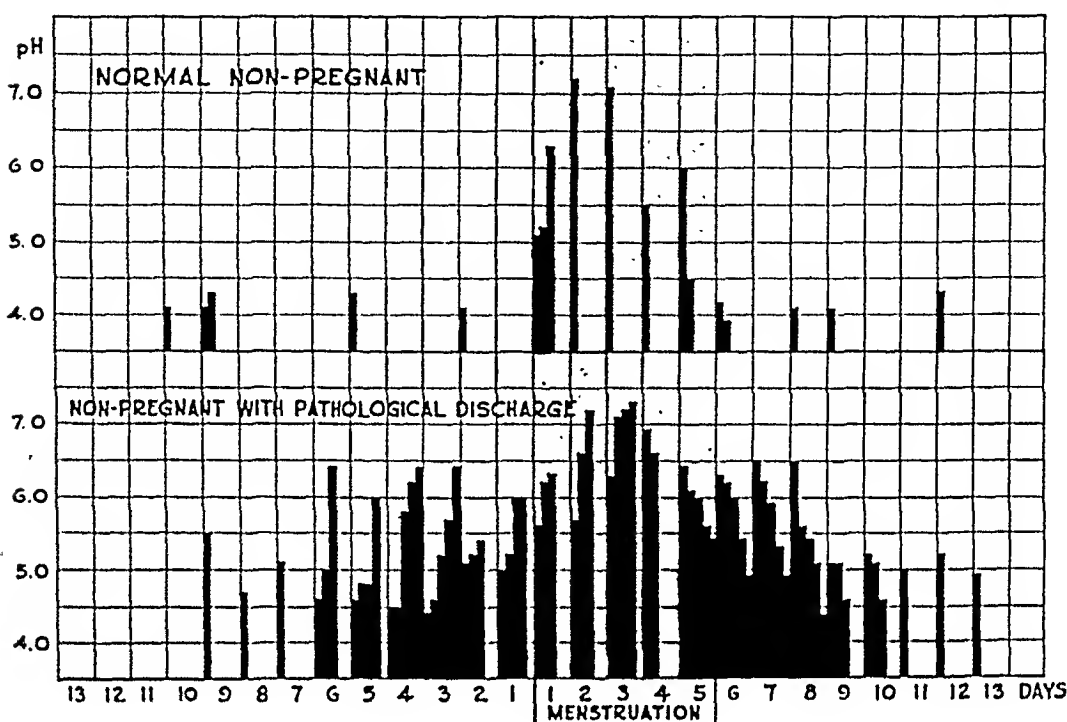


Fig. 3.

CYCLIC CHANGES OF VAGINAL DISCHARGE (OF... AGE 25)

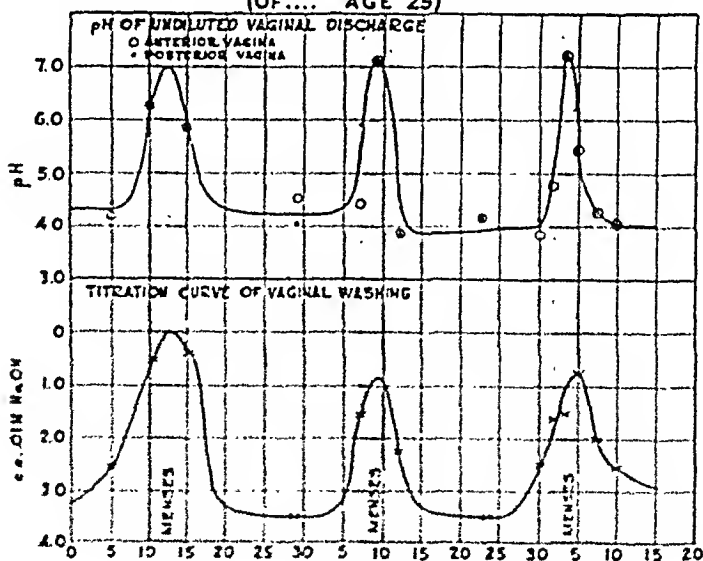


Fig. 4.

obtained from the various titration values. These data indicate a definite cyclic variation in the vaginal acidity during each lunar month, with a significant increase in the pH during the flow. The fact that the neutral point (pH 7.0) is reached only during the first two or three days of menstruation, when the bleeding is com-

TABLE I. DATA FROM NORMAL NONPREGNANT WOMEN

CASES	ENTIRE PERIOD OF OBSERVATION IN DAYS	NUMBER OF DETERMINA- TIONS	AVERAGE pH		DIFFERENCE IN ANT.-POST. VAGINA	pH RANGE OF ENTIRE VAGINA	C.C. OF .01 N NaOH USED TO NEUTRALIZE 20 C.C. VAGINAL WASHING		
			ANTERIOR VAGINA	POSTERIOR VAGINA			AVERAGE	RANGE	
<i>A. Intermenstrual</i>									
O. F.	65	2	4.14	4.12	+0.02	3.86-4.59	2.67	2.0-3.5	
O. D.	15	4	4.25	4.25	+0.00	4.00-4.51			
<i>B. Menstrual</i>									
CASES	DATE OF MENSTRUAL PERIOD	DATE OF DETERMINATIONS	AVERAGE pH		DIFFERENCE IN ANT.-POST. VAGINA	C.C. OF .01 N NaOH USED TO NEUTRALIZE 20 C.C. VAGINAL WASHING			
			ANTERIOR VAGINA	POSTERIOR VAGINA					
O. F.	Dec. 10-15	Dec. 10	6.28	6.28	+0.00	0.6			
		Dec. 15	5.97	5.97	+0.00	0.4			
	Jan. 7-11	Jan. 7	4.47	5.97	-1.45	1.5			
		Jan. 9	7.07	7.07	+0.00	0.9			
	Feb. 2-6	Feb. 2	4.88	5.73	+0.85	1.7			
		Feb. 3	7.15	7.15	+0.00	1.6			
		Feb. 5	5.45	5.45	+0.00	0.8			

TABLE II-A. DATA FROM NONPREGNANT WOMEN WITH PATHOLOGIC DISCHARGE, INTERMENSTRUAL PERIOD

NAME	ENTIRE PERIOD OF OBSERVATION IN DAYS	NUMBER OF DETERMINATIONS [†]	AVERAGE pH		DIFFERENCE IN ANT-POST. VAGINA	pH RANGE OF ENTIRE VAGINA	REMARKS
			ANTERIOR VAGINA	POSTERIOR VAGINA			
<i>A. Intermenstrual</i>							
E. K.	4	3	5.48	5.46	+0.02	4.85-5.83	Gonorrhea and latent syphilis
B. S.	4	4	—	4.75	—	4.60-4.95	Gonorrhea
B. E.	26	14	4.95	6.50	-1.55	4.28-7.57	Gonorrhea with arthritis
H. M.	19	10	4.71	4.86	-0.15	4.40-6.09	Gonorrhea, treatment
K. W.	5	5	5.79	5.83	-0.04	5.05-6.64	Gonorrhea with arthritis
O. B.	17	10	5.48	5.23	+0.25	4.80-6.29	Gonorrhea, treatment
	5	4	4.67	4.62	+0.05	4.41-5.02	Gonorrhea, treatment, one month later
Z. M.	1	1	6.09	—	—	—	Gonorrhea
N. C.	1	1	6.30	—	—	—	Neurosyphilis
G. E.	1	1	5.14	—	—	—	Gonorrhea and syphilis
M. C.	1	1	4.77	—	—	—	Neurosyphilis
W.	3	2	5.69	5.61	+0.08	5.36-6.17	Gonorrhea
L. A.†	8	3	6.56	—	—	6.49-6.60	Gonorrhea, child, aged 7 years
Average		56	5.17	5.73			

*These determinations were distributed equally through the intermenstrual period.

TABLE II-B. DATA FROM NONPREGNANT WOMEN WITH PATHOLOGIC DISCHARGE, MENSTRUATION NOT INCLUDED IN THE AVERAGE

CASES	DURATION OF MENSTRUATION IN DAYS	NUMBER OF DETERMINATIONS	AVERAGE pH		DIFFERENCE IN ANT.-POST. VAGINA	pH RANGE OF ENTIRE VAGINA	REMARKS
			ANTERIOR VAGINA	POSTERIOR VAGINA			
B. Menstrual							
B. S.	4	1	-	7.32	-	-	Gonorrhea
B. E.	4	3	6.41	7.37	-0.96	5.10-7.43	Gonorrhea with arthritis
H. M.	7	6	5.34	6.89	-1.15	4.82-7.69	Gonorrhea, treatment
O. B.	7	7	6.07	6.55	-0.48	5.22-7.52	Gonorrhea, treatment
	6	1	5.58	6.36	-0.78	5.58-6.36	Gonorrhea, treatment, one month later (last day of men- struation)
Average	6	18	5.84	6.82			

monly more profuse, suggests that the actual flow of blood may be responsible. Since blood is alkaline (pH 7.4), it may neutralize the acid more or less completely while the actual discharge is removing the acid mechanically. The vaginal flora apparently reacts to this changed reaction by a marked reduction in the number and proportion of the vaginal bacilli even in women who have normally a Type I discharge.

Pregnant Women With Normal Discharge (Type I).—A total of 44 determinations were made upon 8 normal pregnant women during the last eleven weeks of gestation. The pH range, 4.02 to 5.49, was slightly higher than in the normal nonpregnant group, and the average, pH 4.76, was also somewhat higher (Table III). Microscopically, it was noted that the number of epithelial cells was increased while there was no apparent change in the leucocytes. The average specimen from the upper vagina showed a pH slightly lower than that from the lower vagina in spite of the augmented cervical secretion which normally accompanies gestation and which might have been expected to make the upper vagina more alkaline.

TABLE III. DATA FROM PREGNANT WOMEN WITH NORMAL DISCHARGE

CASES	DURATION OF EXPERIMENT IN DAYS	NUMBER OF DETERMINATIONS	AVERAGE pH		DIFFERENCE IN ANT-POST. VAGINA	pH RANGE OF ENTIRE VAGINA	REMARKS
			ANTERIOR VAGINA	POSTERIOR VAGINA			
J. W.	35	25	4.95	4.96	-0.01	4.60-5.49	29-38 weeks pregnant
F. C.	1	1	4.35	—	—	—	31 weeks pregnant
E. B.	1	1	5.06	4.59	+0.47	4.59-5.06	40 weeks pregnant (delivered 5 hours later)
J. R.	1	1	4.42	4.34	+0.08	4.34-4.42	31 weeks pregnant
A. K.	1	1	4.18	4.38	-0.20	4.18-4.38	29 weeks pregnant
D. P.	17	3	4.39	4.26	+0.13	4.13-4.70	32-35 weeks pregnant
L. C.	39	8	4.49	4.19	+0.30	4.02-4.91	29-35 weeks pregnant
N. W.	9	2	4.77	4.74	+0.03	4.56-4.92	32-35 weeks pregnant
Average		44	4.76	4.68			

TABLE IV. DATA FROM PREGNANT WOMEN WITH PATHOLOGIC DISCHARGE

CASES	DURATION OF EXPERIMENT IN DAYS	NUMBER OF DETERMINATIONS	AVERAGE pH		DIFFERENCE IN ANT-POST. VAGINA	pH RANGE OF ENTIRE VAGINA	REMARKS
			ANTERIOR VAGINA	POSTERIOR VAGINA			
G. C.	1	1	5.74	6.00	-0.25	5.75-6.00	21 weeks pregnant. Gonorrhea, leucorrhoeal discharge, profuse
F. H.	41	9	5.54	5.70	-0.16	5.23-6.01	20-26 weeks pregnant. Clinical gonorrhea
H. W.	9	3	4.82	4.48	+0.32	4.24-5.04	26 weeks pregnant. Clinical gonorrhea. Treatment
T. M.	1	1	4.53	-	-	-	23 weeks pregnant. Clinical gonorrhea
E. R.	57	27	5.21	5.10	+0.11	4.58-6.09	27-36 weeks pregnant. Gonorrhea and Wassermann negative. Profuse discharge, eosin, chronic cervicitis
Average		41	5.25	5.02			

TABLE V. CHANGES IN pH OF THE VAGINAL DISCHARGE EFFECTED BY DILUTION WITH NEUTRAL WATER

CASES	UNDILUTED DISCHARGE		VAGINAL WASHING 15 C.C. WATER	pH AFTER FURTHER DILUTION OF THE VAGINAL WASHING BY ADDITION OF SUCCESSIVE 5 C.C. PORTIONS OF NEUTRAL WATER	REMARKS
	ANTERIOR VAGINA pH	POSTERIOR VAGINA pH			
E. K.	6.6	6.15	6.90	7.00, 7.12, 7.10, 7.10	Nonpregnant, gonorrhea and syphilis
E. K.	-	5.67	5.80		Nonpregnant, gonorrhea and syphilis
E. K.	-	6.00	6.63	6.88, 7.12, 7.22	Nonpregnant, gonorrhea and syphilis
B. S.	-	7.45	7.13		Nonpregnant, gonorrhea, menstruation
B. S.	-	5.08	6.18		Nonpregnant, gonorrhea
W.	6.17	6.15	6.34	6.47, 6.50, 6.57, 6.67	Nonpregnant, gonorrhea
W.	5.50	5.36	5.47	5.57, 5.82, 6.05, 6.18	Nonpregnant, gonorrhea
F. H.	5.37	5.87	5.67	5.87, 6.25	20 weeks pregnant, gonorrhea
F. H.	5.80	6.04	5.90	6.10, 6.25, 6.42, 6.55, 6.80	20 weeks pregnant, gonorrhea
F. H.	5.46	5.65	5.12	5.12	21 weeks pregnant, gonorrhea
F. H.	5.53	5.88	5.73	5.75, 5.79, 6.00, 6.10, 6.23, 6.34	22 weeks pregnant, gonorrhea
H. W.	4.60	4.37	4.28	4.45, 4.72	26 weeks pregnant, gonorrhea
H. W.	4.78	4.78	4.52	4.60, 4.76	26 weeks pregnant, gonorrhea
T. M.	-	4.64	4.95		23 weeks pregnant, gonorrhea
B. P.	4.42	4.52	4.38	4.42, 4.55, 4.62, 4.98, 5.60	33 weeks pregnant, normal
L. C.	4.57	4.32	4.15	4.35	29 weeks pregnant, normal
L. C.	4.75	4.20	4.10	4.20, 4.32, 4.50, 4.68, 5.07, 5.40	31 weeks pregnant, normal
L. C.	4.30	4.65	4.40	4.95, 5.40, 5.73, 6.00, 6.11	32 weeks pregnant, normal

Pregnant Women With Abnormal Discharge (Types II and III).—Forty-one determinations upon five women twenty-six to thirty-six weeks pregnant and showing clinical evidence of gonorrhea showed a pH range of 4.24 to 6.09, and an average of pH 5.25 for the lower vagina and of pH 5.02 for the upper portion (Table V). The tendency toward a reduced acidity was exhibited by all the patients studied and may be viewed as a direct result of the infection.

Fig. 5 shows graphically the individual readings in the group of pregnant women according to the bacteriologic character of the discharge. The preponderance of pH readings below 5.0 in those with a normal flora is very evident. There was no evidence of cyclic changes indicative of a continuance of the menstrual variations.

The Effect of Dilution With Neutral Water.—The effect of dilution was determined on eighteen specimens by washing the vagina with 15 c.c. of neutral distilled water after material had been collected in the usual fashion directly into the electrode point. When the pH of this wash fluid had been determined, further dilutions with 5 c.c. portion were effected in fourteen instances. The original wash fluid usually, but not invariably, showed a pH somewhat lower than that of the undiluted dis-

pH OF VAGINAL DISCHARGE DURING GESTATION

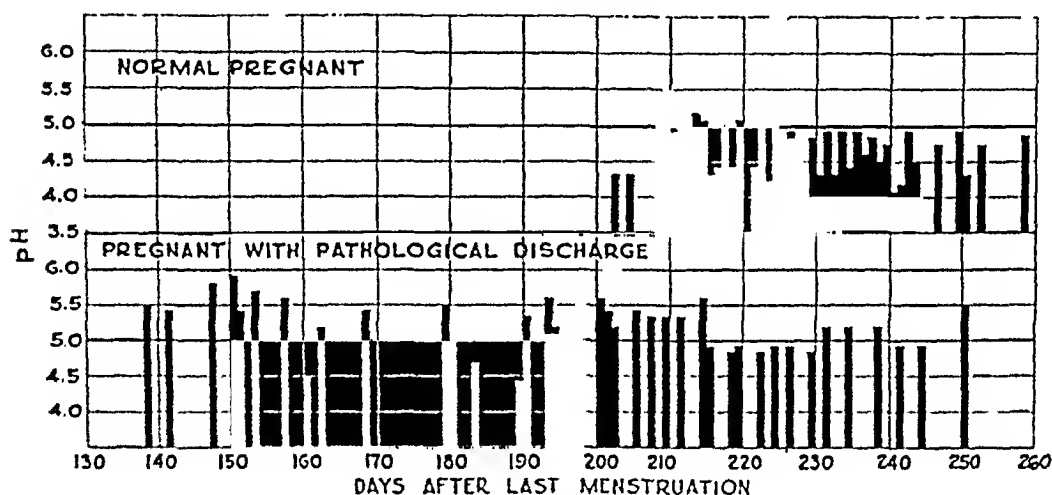


Fig. 5.

charge, whereas further dilution always reduced the acidity. Such equivocal findings are not easily explained, but they suggested that the acidity of the discharge may vary considerably from place to place on the mucosa and that the direct readings may vary accordingly. With this possibility in mind it would seem that for general purposes the pH of wash fluid may be more accurate than the reading obtained from small undiluted portions of the discharge.

SUMMARY

The available literature on vaginal acidity is reviewed.

A quinhydrone microelectrode for the determination of the pH of undiluted vaginal discharge is described and its operation detailed.

The pH of the vaginal discharge varies directly with the character of the vaginal flora, higher acidities being associated with a preponderance of the vaginal bacilli of Döderlein which are normally present in pure culture but may be entirely absent in certain infections (gonorrhea).

The vaginal discharge is normally quite acid (pH 4.0 to 4.5) during the intermenstrual period but approaches or exceeds neutrality during the early days of menstrual bleeding.

During gestation the acidity is somewhat less than in the nonpregnant, irrespective of the bacterial character of the discharge.

The pH of the upper (posterior) vagina is usually slightly lower than that of the lower (anterior) portion.

Dilution of the vaginal discharge with neutral water tends to raise the pH although the acidity of vaginal washings may be higher than that of the undiluted discharge.

CONCLUSIONS

The reaction of the vagina is normally acid but the degree of acidity varies with the character of the flora as well as with the physiologic changes induced by menstruation and gestation.

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A STUDY OF THREE HUNDRED AND EIGHT CASES OF PLACENTA PREVIA*

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SINCE placenta previa results from a simple anatomic anomaly in the implantation of the ovum and is usually unassociated with any other morbid condition, it should, in most instances, present no great obstacle to a successful outcome. Provided that the patient has not been infected by examination or vaginal packing under unsterile conditions, the risk of serious sepsis should not be great. Unlike the complicated variety of premature separation of the normally implanted placenta, the picture is seldom darkened by the coexistence of toxemia or nephritis, and shock from distention of the uterus by concealed hemorrhage is not a factor. Aside, then, from previous hemorrhage, which may be remedied by transfusion, the problem when the patient is first seen resolves itself into the question of how best she may be delivered without losing more blood, and at the same time, how may a living child be obtained for her, if such a thing is possible. As concerns the infant, the outlook is not always bright, since one-fourth of the babies in our series weighed less than 4 pounds, and over one-third were born before the thirty-fifth week of gestation. Moreover, about one-seventh of our 315 infants were dead on admission to the hospital. If the mother is uninfected and her baby is normal and of reasonable size and maturity, the method of delivery, which will secure the best outlook for the child, should be selected, always provided that the mother is subjected to no extra risk thereby. If the child is dead, or if it is malformed or under 4 pounds in estimated weight, it is not an element in the problem. Moreover, the story does not end with the current pregnancy. Although it is most unlikely that the patient will have another placenta previa in a later gestation, the type of delivery employed in the present crisis may have a marked bearing upon her obstetric future. Of our 80 patients delivered by cesarean section, 7 were subjected to the same operation in the next pregnancy because, on account of febrile puerperia, it was feared that rupture of the uterus might supervene if they were allowed to go through labor. It is evident, therefore, that cesarean section should not be a routine method of delivery in placenta previa. In this complication of pregnancy, as in many others, there is no one treatment for every patient.

*Read (by invitation) at a meeting of the Chicago Gynecological Society, December 26, 1916.

From Jan. 1, 1916, to Jan. 1, 1935, among 28,391 deliveries on the In-Patient Service of the Boston Lying-In Hospital, there were 308 consecutive cases of placenta previa, a frequency of 1 in every 92 confinements. During approximately the same period, premature separation of the normally implanted placenta occurred once in every 96 deliveries; an almost equal incidence. Since it is the general impression that in private practice placenta previa occurs about once in every 500 deliveries, it is apparent that our experience with this complication exceeds five times the normal expectancy. Provided there is a bed available, the hospital never refuses a patient referred by an outside physician. While this situation makes it impossible for us to expurgate, or rather, improve our statistics by refusing the unfavorable cases, it supplies us with ample teaching material and provides a constant challenge to the staff. The actual delivery of these 308 patients was conducted by 85 visiting and resident obstetricians, the latter always under supervision.

The nineteen years under study divide themselves naturally into three periods: the eight years from 1916 to 1923 inclusive when there were 105 cases, the six years from 1924 to 1929 inclusive when there were 103, and the five years from 1930 to 1934 inclusive when there were 100 patients with placenta previa. These three periods are interesting historically, since they show the changing trends in an American clinic. The last period, from 1930 to the beginning of the present year, is of particular significance, as it marks the improvement wrought through concerted action by the whole staff in carrying out a predetermined policy.

Before we discuss the methods of treatment employed and the maternal and fetal mortality in each period, it may be of interest to indicate certain general considerations which were brought to light in the analysis of these 308 cases.

GENERAL CONSIDERATIONS

The Effect of Multiparity.—There were 274 multiparas and 34 primiparas, a preponderance of 8 to 1. Since the usual ratio of multiparas to primiparas in the clinic is about 6 to 4, there can be no question that multiparity has a striking effect upon the incidence of placenta previa. In our comparable series of 284 cases of premature separation of the normally implanted placenta, we found only two and one-half times as many multiparas as primiparas.

Placenta previa does not tend to repeat itself in subsequent pregnancies, since none of our patients were again admitted for the same condition. For this reason the familiar theory of Strassmann, that many and frequent pregnancies produce a chronic endometritis and so encourage placenta previa, does not appear to rest on secure ground, since, were it true, we should have had several recurrences in a series of this size. As regards the association between low implantation of the placenta and multiparity, there seems to be some unknown biologic factor at work. With primiparas there is apparently a greater tendency toward fundal implantation. In inversion of the uterus where fundal attachment is common, the incidence is equally divided between primiparas and multiparas.

Condition of the Fetus.—Of the 315 infants born in the 308 deliveries, there being 7 pairs of twins, the birth weights of 286 were recorded. Seventy-one or 24.9 per cent weighed less than 4 pounds. One hundred and sixteen of the 315 infants or 37 per cent were born before the thirty-fifth week of gestation, and 48 or 15.2 per cent were dead when the patient entered the hospital. Prematurity, underdevelopment, and uterine death thus exert their malign effects upon the infants of women with placenta previa. There is always an intrinsic danger to the fetus, whatever may be the method of delivery.

Twins occurred about twice as often as is the normal expectancy. The incidence was one pair in every 44 deliveries, and the usual frequency is one in every 87. Fetal abnormalities were somewhat more common than usual, there being one case each of hydrocephalus and anencephalus. In our clinic hydrocephalus occurs once in every 581 deliveries and anencephalus once in every 470 deliveries. There was one case each of syphilis and erythroblastosis fetalis.

Types of Placenta Previa.—Of the 308 cases, 77 or 25 per cent were complete, 97 or 31.5 per cent were partial, and 134 or 43.5 per cent were marginal. There were 22 deaths in the entire series of 308 cases. Eleven occurred in the 77 complete previas, a mortality in this type of 13 per cent; 8 in the 97 partial previas, or 8.2 per cent; and 3 in the 134 marginal variety, or 2.2 per cent. These figures bear out the general impression regarding the relative danger of the three types, except that complete previa proved to be only about one and one-half times as fatal as the partial variety.

Vaginal Examination.—Two hundred and eighty-seven, or 93.2 per cent of the 308 patients were examined vaginally. It is difficult to see how a definite diagnosis can be made in any other way. In the 21 cases that were not so examined, the patients were bleeding freely on entrance, the fetal hearts were heard and the infants seemed of sufficient size to survive. Cesarean sections were performed forthwith, since the diagnosis in each case lay between placenta previa and partial premature separation of the placenta, and abdominal delivery was equally good treatment in either event.

All vaginal examinations of bleeding cases are made with the patient under anesthesia and with the operating room, instruments, assistants, and nurses, ready for a Braxton Hicks version, insertion of a bag, or cesarean section. We once lost a patient through neglect of these precautions and do not intend to have it happen again. Rectal examinations are forbidden. They give no definite information and may dislodge the placenta sufficiently to produce a dangerous hemorrhage when the operator is in no position to arrest it.

Transfusion was employed 47 times; 10 times before, 7 times during, and 30 times after delivery. Nineteen patients were transfused once and 14 twice. No argument need be advanced concerning the beneficial effect of transfusion. Immediately on the arrival of a patient with placenta previa, one or more compatible donors should be obtained and held in readiness. It is our policy to have one donor on hand ahead of our immediate needs until it is evident that the patient will need no more blood.

The Intrauterine Pack.—The intrauterine gauze pack was used in 30 patients. It is noteworthy that tamponade was considered necessary only once in our latest group of 109 patients delivered in the past five years.

CHRONOLOGIC GROUPS

The first period covered the eight years from Jan. 1, 1916 to Jan. 1, 1924, and included 105 cases. Chart 1 shows that the maternal mortality was 7.6 per cent and the net fetal mortality 47 per cent. By net fetal mortality is meant the stillbirth or neonatal death of any infant that is

alive *in utero* when the patient enters the hospital, that has a birth weight of 4 pounds or over and is not malformed. Such an infant we

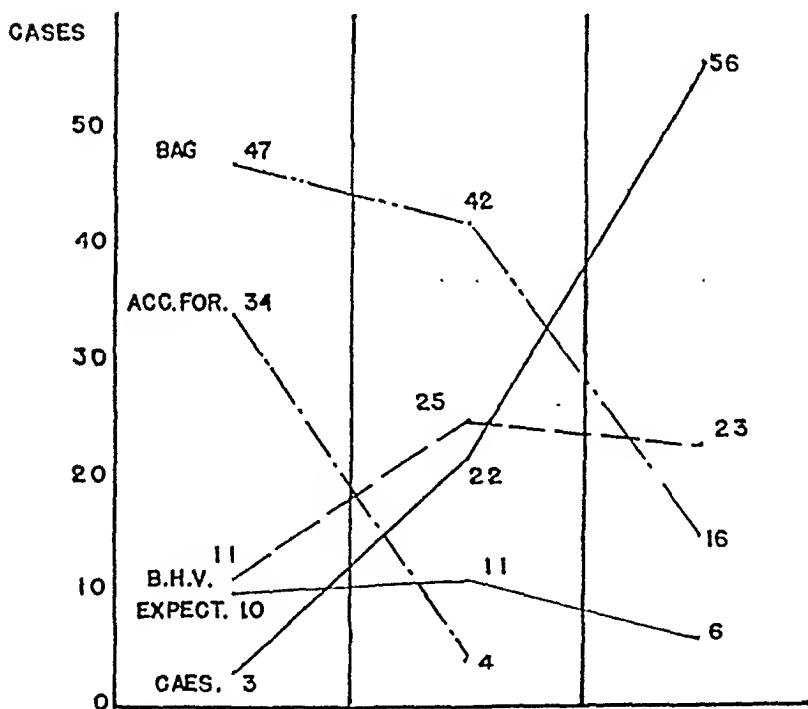
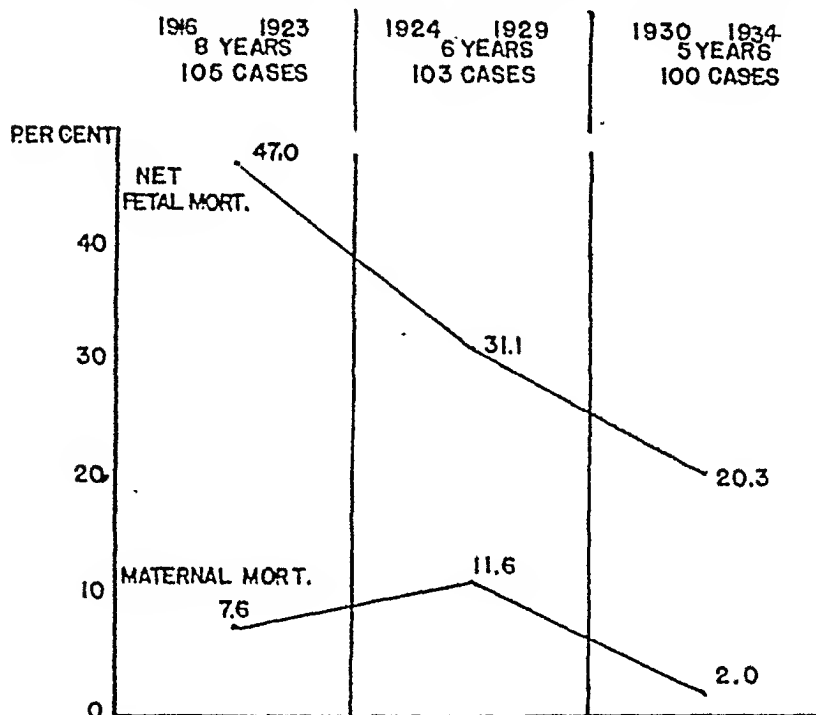


Chart 1.—Placenta previa at the Boston Lying-In Hospital considered chronologically. A, Net fetal mortality and gross maternal mortality. B, Various methods of delivery; number of cases.

believe has a reasonable chance of survival. Since almost half of the infants that might have lived succumbed, it would seem that during

these eight years the baby was little better than a by-product. The maternal mortality of 7.6 per cent was not discreditable at the time, Wagner reporting one of 9.3 per cent, Lieberman, 13.8 per cent, and Miller, 20 per cent.

The reason for the high fetal mortality may be found in Chart 1 which shows the methods of delivery in use. Eighty-one of the 108 patients were delivered after insertion of the Voorhees' bag or by manual dilatation and extraction. Eleven Braxton Hicks versions were performed, 10 patients, all cases with marginal implantation, were subjected to simple rupture of the membranes or extraction at full dilatation, and there were only 3 cesarean sections. It would appear that the unsatisfactory results during this period were due to *accouchement forcé*, the use of the metreurynter or both. The maternal and fetal mortalities attendant upon these methods of delivery will be taken up in detail when the various methods of treatment are discussed.

In the second period, from Jan. 1, 1924, to Jan. 1, 1930, six years, 103 patients were delivered. By this time *accouchement forcé* had acquired an evil reputation and only four such deliveries occurred. The bag was used about as many times as in the previous group but Braxton Hicks version had doubled in frequency and cesarean section had increased sevenfold. The net fetal mortality had dropped 16 per cent, but the maternal mortality had risen 4 per cent to 11.6. The cause of the even more unsatisfactory death rate, therefore, lay possibly in the increased number of cesarean sections or Braxton Hicks versions or in the only slightly diminished number of Voorhees' bag inductions. When we study the effects in the entire series of the various methods of delivery, we shall see that the improper use of the bag was not only during this period, but at other times, productive of consistently poor results.

Beginning with the last period, from Jan. 1, 1930, to the beginning of this year, the staff has developed and carried out a definite policy as regards placenta previa. All clean cases are divided into two classes: (1) Those whose infants have a good expectation of survival. Such patients are delivered by cesarean section, almost always of the classical type. (2) Those whose infants are dead, or under 4 pounds in estimated weight or where gross malformations are shown by the x-ray. With these individuals the baby need receive no consideration. If the cervix is dilated sufficiently to admit two fingers, a Braxton Hicks version is performed. If the cervix is not two fingers dilated, the membranes are ruptured or the placenta perforated, and a Voorhees' bag is inserted. Following the expulsion of the bag a Braxton Hicks version is performed or, if the patient is progressing normally and is not bleeding, she is allowed to deliver herself. In any event no attempt at extraction is made, and the patient is allowed to expel the fetus by her own unaided efforts. (3) If the patient is infected, as shown by fever and a

foul discharge, or if the patient enters with cotton or other unsterile packing in the vagina, a cesarean section is performed followed by a hysterectomy with drainage whatever may be the condition of the fetus.

Following the adaption of this policy the number of patients treated by the Voorhees' bag alone fell from 42 in the preceding group to 15, cesarean sections increased two and a half times, and the number of Braxton Hicks versions remained about the same. The net fetal mortality dropped to 20.3 per cent. The maternal mortality fell to 2 per cent, both deaths occurring in the 56 cesarean sections. In the last fifteen years, therefore, the maternal mortality has been reduced to one-fifth of its highest point and the net fetal mortality over one-half.

METHODS OF TREATMENT

A general analysis of the various types of treatment used in the entire series of 308 cases shows that they may be classified as (1) expectant, consisting of simple rupture of the membranes, or normal or operative delivery at full dilatation, (2) cesarean section, (3) Braxton Hicks version, (4) the Voorhees' bag, and (5) *accouchement forcé*.

Expectant treatment.—Twenty-one cases fall into this group. Eighteen were marginal and 3 partial. None were of the complete variety. In 10 instances the membranes were ruptured artificially and 11 infants were born, there being one pair of twins. Seven were delivered normally, 3 by forceps and 1 by version. Eleven other patients had a normal first stage without any interference, and eleven infants were delivered at full dilatation, 3 normally, 6 by version, 1 by forceps, and 1 by breech extraction. All of the mothers survived. The gross fetal mortality was 8 deaths in 22 infants or 36.4 per cent. The net fetal mortality, however, was 1 death among the 14 infants that might have survived, or 7.1 per cent. The percentage of patients having febrile puerperia, that is, a temperature of 100.4° on any two successive days after delivery, was 1 case in 21, or 4.8 per cent. Although the gross fetal mortality in expectant treatment has been given at 41 per cent by Watson and 42.3 per cent by Burgess, the low net fetal death rate will encourage us to adopt in the future this extremely conservative policy in cases of marginal implantation, particularly when the patient is in labor or the cervix shows beginning dilatation.

Cesarean Section.—Eighty patients were delivered by cesarean section. The classical operation alone was performed 59 times. On 9 other occasions it was followed by tubal sterilization and 5 times by hysterectomy. In one instance the uterus was extraperitonized by suture to the abdominal wall before incision, and on another occasion a drain was placed to the uterine wound as a precautionary measure. Five lower segment operations were performed, 4 of the Kerr or transverse incision type, one being followed by a hysterectomy, and one of the Kroenig or vertical incision variety. Although our experience with lower segment operations in placenta previa has been small, our present preference is for the corporeal incision since it enables us to avoid the placental site. Four of the patients delivered by cesarean section died, giving a mortality of 5 per cent; one died of hemorrhage during the operation, 3 of hemorrhage afterward, and one of intestinal obstruction six days postpartum. The maternal morbidity was 40.3 per cent, by far the highest in the series. The gross fetal mortality was 23.5 per cent which is the lowest by any method of treatment. This figure reflects the policy of the clinic, which reserves abdominal delivery for those patients with a good expectation of a living infant. The net fetal mortality was 13.7 per cent, which, next to that obtained by expectant treatment, is again the

lowest in our series. Thirty-one of the patients delivered by cesarean section had complete placenta previa, 29 partial and 20 marginal. In selecting cesarean section the viability of the child influenced us more than the type of previa.

Braxton Hicks Version.—Braxton Hicks version can be performed only when the cervix is at least two fingers dilated. The membranes are ruptured or the placenta perforated, the head displaced upward and a foot brought down by combined vaginal and abdominal manipulation. Once turned, the expulsion of the fetus is left entirely to nature. Combined version followed by the so-called slow extraction is nothing but *accouchement forcé* and is attended by the same risk of cervical laceration, shock and hemorrhage. As long ago as 1860 Hicks warned against this error. Almost all textbooks on obstetrics advise Braxton Hicks version for the general practitioner, but make no mention of the technical difficulties that the operation sometimes presents. After a moderately extensive experience with this procedure, I still find it difficult on occasions, and I consider the suggestion that it be employed by untrained men to be exceedingly bad advice. Once the baby is turned, however, the half breech effectively tampons the placental site and all bleeding ceases. This is true in every case.

It was necessary in 8 of our 56 cases to secure at least two fingers' dilatation by the preliminary use of the bag before Braxton Hicks version could be accomplished. Sixteen patients had complete placenta previa, 23 partial and 17 marginal. Since the gross fetal mortality is extremely high, being 84.5 per cent in this group, this method of delivery is suited only for the infant whose chances of life are not good; in other words, the dead, premature, or deformed fetus. The net fetal mortality was also high, being 59 per cent, since we lost 13 of the 22 infants that had a reasonable expectation of life. This shows that cesarean section would have been a better operation for the baby in these cases, and that we made an unwise selection of the method of delivery. Braxton Hicks version creates no prejudice as to the form of delivery in succeeding pregnancies. Four of the 56 patients were delivered once subsequently in the clinic, two twice, and one four times, all normally.

There were 3 maternal deaths following Braxton Hicks version, a mortality of 5.3 per cent, which is about the same as in cesarean section. Two of the women died from puerperal sepsis. Both were infected emergency cases and should have been subjected to the Porro operation. The third died on the twelfth day of encephalitis lethargica. It will be noted that there were no deaths from hemorrhage. The maternal morbidity was 23.2 per cent, which is considerably lower than that of cesarean section.

The Voorhees' Bag.—In 111 patients delivery was accomplished through the use of the Voorhees' bag. Eighteen had complete previas, 31 partial, and 62 marginal. Eight of these women died, giving a mortality of 7.3 per cent. Five fatalities were due to hemorrhage, 2 to sepsis, and 1 toxic patient died undelivered. Since the use of the metreurynter is generally considered conservative obstetrics, it is at first glance not evident why the death rate should be higher than in cesarean section or Braxton Hicks version. A study of our cases, however, points out the reason. Twenty-four patients, all with marginal previas, were delivered normally after the use of the bag, and none of them died. There were 3 fetal deaths or a gross mortality of 12.5 per cent. Aside from the toxemic patient who died undelivered, the remaining 85 were subjected to some pelvic operative procedure after expulsion or removal of the bag and 7 of them died, giving a mortality of 8.1 per cent for this sub-group. Fifty-nine were delivered by internal podalic version with 6 deaths, 15 by breech extraction with 1 death and 12 by forceps without fatality. It is, therefore, evident that as regards the Voorhees' bag the entire mortality depended upon operative delivery, undoubtedly undertaken before the cervix was completely out of the way, resulting in laceration, hemorrhage, and shock.

Of the bag cases the 105 surviving patients had a morbidity of 16.2 per cent. The gross fetal mortality in all patients delivered by this method was 54.0 per cent, and the net fetal mortality was 28 per cent.

The bag may prove a menace unless it is used with extreme caution. With marginal previa, in our experience at least, it will give no better results for the mother than simple rupture of the membranes and over twice as high a net fetal mortality. We now use it chiefly as a preliminary to Braxton Hicks version in cases where there is not sufficient cervical dilatation.

Accouchement forcé is reserved for final consideration since it recalls the darkest days of placenta previa. Thirty-eight patients were so delivered, seven of them died, resulting in a mortality of 18.4 per cent. Six patients died from hemorrhage and one from sepsis. The morbidity of the 31 surviving patients was 22.6 per cent. Among the patients delivered by *accouchement forcé* the gross fetal mortality was 64.1 per cent, and the net fetal mortality was 39.5 per cent.

No comparable number of cases can be reported without evidences of some originality on the part of one or more operators. The Willett forceps were applied to the fetal scalp on 3 occasions. They slipped off in every instance, and it was necessary to complete delivery by another method. One vaginal cesarean section was performed for reasons not apparent in the record. The mother survived. Equally obscure is the reasoning of several German authors who still advocate this operation. To us it would seem a deliberate invitation to disaster.

There remain to be considered the general questions of maternal mortality, maternal morbidity, fetal mortality, and in conclusion, the lessons learned from the analysis of the entire series.

MATERNAL MORTALITY

In the 308 cases there were 22 deaths, an uncorrected mortality of 7 per cent. Fifteen succumbed to hemorrhage, 4 to sepsis, and 1 each to intestinal obstruction, toxemia, and encephalitis lethargica. In the light of our present knowledge the deaths from hemorrhage may be greatly reduced, and those from sepsis practically eliminated by cesarean section and hysterectomy in the neglected emergency case (Chart 2).

The last 100 cases in our series show the beneficial effects of a systematic policy, since our mortality has fallen to 2.0 per cent. This has apparently resulted from an increase in cesarean section and a decrease in the employment of the Voorhees' bag. The useful operation of Braxton Hicks version is employed in every fourth or fifth case.

Our lowered mortality is in keeping with progress in other clinics. Bill reports a death rate of 1.92 per cent in 104 cases, Greenhill a rate of 2.6 per cent in 118 cases, Rucker 3.5 per cent in 141 cases, and Dailey no deaths among 139. It is significant that in the series reported by these writers cesarean section was not the method selected in the majority of cases and that many were delivered through the pelvis by conservative measures.

MATERNAL MORBIDITY

Cesarean section shows the highest percentage of fever in the puerperium, and simple rupture of the membranes the least. That this frequent rise in temperature following abdominal delivery does not indicate peritonitis is shown by the fact that none of the 80 patients died from this cause (Chart 3).

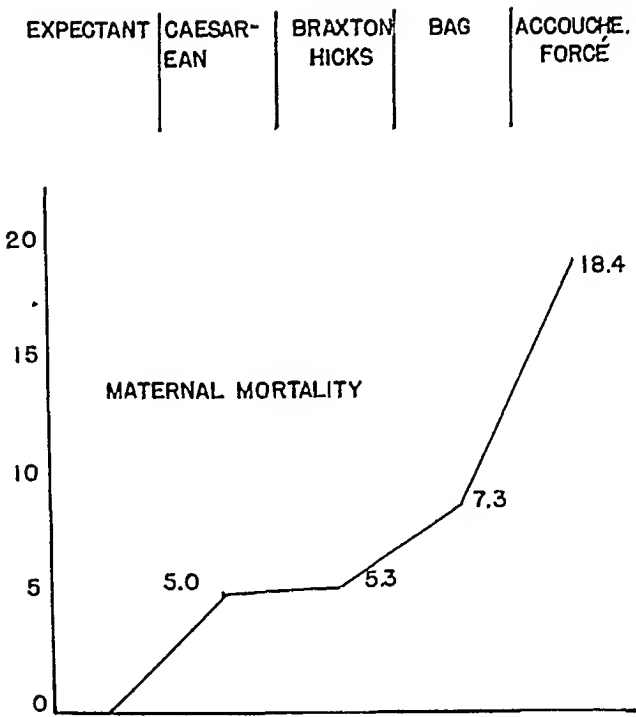


Chart 2.—Percentage maternal mortality in various methods of delivery.

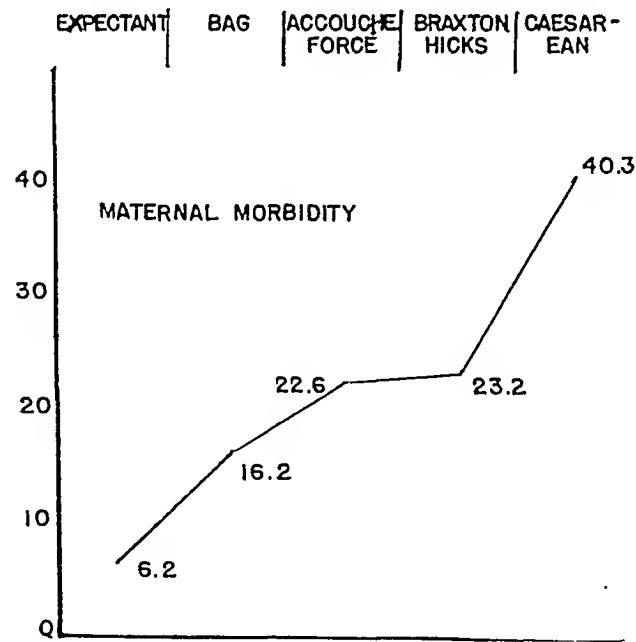


Chart 3.—Percentage maternal morbidity in various methods of delivery.

FETAL MORTALITY

Since, as we have already seen, many of the infants are either dead on admission to the hospital or premature, the gross mortality can be influenced only by reduction of the net mortality. Other things being equal a baby that is alive, of an estimated weight of four pounds or more, and not malformed in cases of complete or partial previa should be delivered by cesarean section, since the net fetal death rate is only 13.7 per cent. When the baby cannot be saved by any method of delivery, cesarean section is no better for the mother than Braxton Hicks version. Cesarean section is the baby's operation, not necessarily the mother's. This policy should apply to expert obstetricians only. The occasional or untrained accoucheur who encounters a case of placenta previa in a small community will best serve his patient's interest

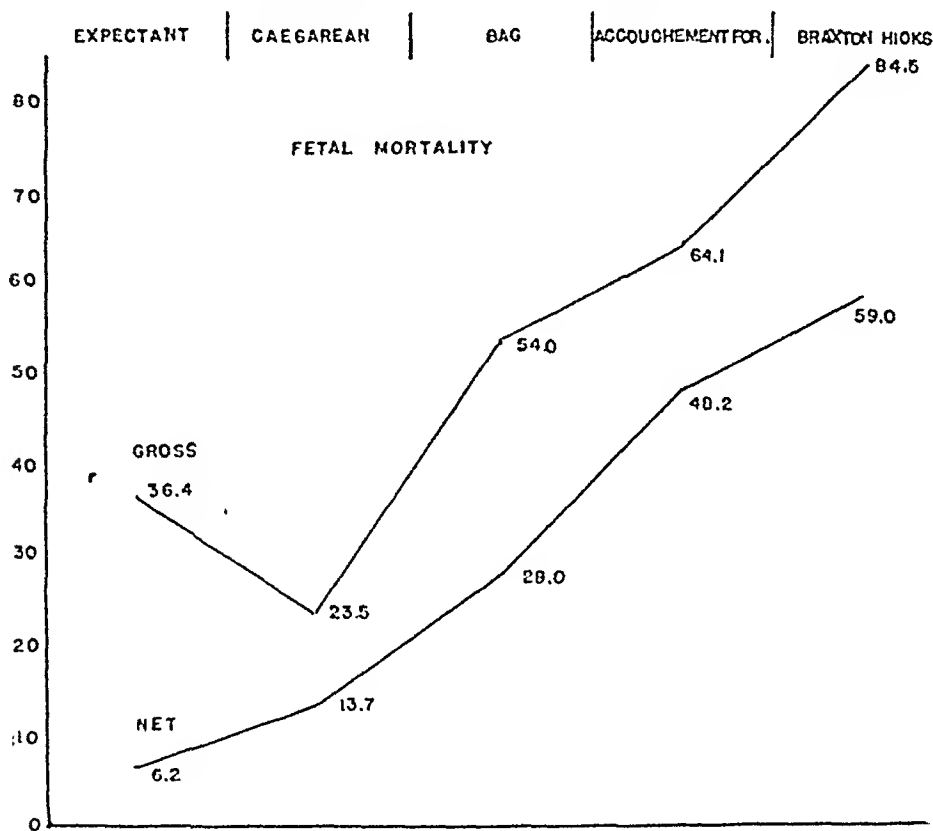


Chart 4.—Percentage gross and net fetal mortality in various methods of delivery.

if he calls in a trained obstetrician if there be one available. In the absence of such aid his second choice is to invite a surgeon to perform a cesarean section regardless of the state of the baby.

In the last 100 cases we have secured a net fetal mortality of 20.3 per cent, which approaches our net mortality of 13.7 per cent in cesarean section, although only 56 patients were subjected to abdominal delivery (Chart 4).

CONCLUSIONS

1. A study of 308 consecutive cases of placenta previa at the Boston Lying-In Hospital shows a decrease in maternal mortality from 11.6 per cent to 2 per cent, and a decrease in net fetal mortality from 47 to 20.3 per cent.

2. In clean cases, where the infant is alive, normal, and of an estimated weight over 4 pounds, cesarean section offers about an 85 per cent chance of securing a living child, with a risk to the mother not exceeding 5 per cent.

3. In clean cases, when the infant is dead, deformed or under 4 pounds in estimated weight, Braxton Hicks version may be performed by the trained obstetrician at no greater risk to the mother than cesarean section.

4. In clean cases of marginal placenta previa, simple rupture of the membranes deserves an extended trial. It is safe for the mother, and apparently less injurious to the child than has been supposed.

5. In infected cases, cesarean section followed by hysterectomy is the operation of choice regardless of the condition of the child.

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DISCUSSION

DR. W. C. DANFORTH.—One point of very great importance which Dr. Irving emphasized and which we adopted some time ago is routine vaginal examination prior to the intervention. It should be done in one place only, however, that is in the place where delivery is to be completed.

No one method for delivery should be employed to the exclusion of all others. I think sometimes there has been an overuse of cesarean section in cases of placenta previa.

Accouchement forcé belongs in the realm of forgotten things, and next to vaginal section seems to be the least rational method of dealing with placenta previa and the one which is most likely to be followed by disastrous results.

Rupture of the bag of waters may be used in a considerable percentage of cases, and many, with no other interference, will go on to a happy termination.

Dr. Irving's view that the bag should be regarded as an instrument for securing a certain amount of dilatation which may or may not be followed by some other operative interference deserves emphasis. In our work the bag is used for that purpose only. Extraction should never follow until dilatation is complete, whether extraction is preceded by version or not. Too early extraction is a form of *accouchement forcé*.

DR. JOSEPH B. DELEE.—We abandoned *accouchement forcé* many years ago, before they did in the East. In 1899 when I visited Williams in Baltimore, he showed me three ruptured uteri, the result of *accouchement forcé*.

You cannot deliver placenta previa cases from below too slowly. We lost one woman from ruptured uterus where during an attempted slow delivery one pain ex-

pressed the shoulders and head. The tear of the cervix extended up into the broad ligaments and into the uterus, the site of a scar from a previous ruptured uterus. She died while receiving a transfusion.

It is not always easy to do a Braxton Hicks version, because you do not attack the operation with sufficient vigor. With the woman completely anesthetized, put one whole hand in the vagina, two fingers through the cervix. If the foot slips away, pass a large volsellum forceps alongside your fingers, grasp the ankle with it and pull a foot down. I have made a special long slender S-shaped forceps with ring ends to grasp the foot, to use in cases of Braxton Hicks version.

The great danger in placenta previa is to the mother, and the baby should be considered secondary. I am willing to state that the high maternal mortality in the United States is partly due to the too high valuation put upon the unborn child. Dr. Peller of Vienna, in a recent study of the mortality rates in Europe, also explains the high maternal mortality on the too high valuation put upon the child.

The placenta previa case should be treated for the benefit of the mother. Even if a monstrosity is diagnosed, it should usually be delivered by cesarean section. The death rate in placenta previa complicated by monstrosities is still too high.

DR. FRED L. ADAIR.—One part of Dr. Irving's observations covers a period corresponding to that of operation of the new Chicago Lying-In Hospital, May, 1931 to November, 1935. We have had 111 cases of placenta previa: marginalis and totalis 43.2 per cent each, and partialis 14 per cent, with no maternal mortality.

Practically 75 per cent of the women were beyond the thirty-sixth week of gestation. The type of placenta previa in relation to the time of gestation was: totalis 35.4 weeks partialis 36.7 weeks, and marginalis 35.7 weeks. The average weight of the fetus was 2,547 gm. in marginalis, 2,000 in partialis, and 2,630 in totalis.

The average estimated antepartum blood loss was 359 c.c., intrapartum and postpartum 410 c.c., and the total loss 769 c.c.

The methods of treatment employed and their percentages were as follows: rupture of the membranes, intentional or unintentional, 13.5; insertion of a bag, 23.4; Braxton Hicks version, 11.7; lower segment cesarean section, 46; and Porro cesarean section, 5.4.

The treatment used in the various types of placenta previa was: rupture of the membranes, in marginalis only; insertion of a bag, in all types but less frequently in totalis; Braxton Hicks version, in all types; lower segment cesarean section, most frequently in totalis; and Porro cesarean section, in both partialis and totalis. Cesarean section was performed in 77 per cent of totalis, in 47 per cent of partialis and 27 per cent of marginalis.

The average weight of the fetus in the cases treated by Braxton Hicks version was 1,774 gm., by insertion of a bag 2,307 gm., by rupture of the membranes 2,563 gm., and by cesarean section 2,939 gm.

The percentage of the fetal mortality in patients treated by cesarean section was 12.3, by rupture of the membranes 33.3, insertion of a bag 50, and Braxton Hicks version 54.

Transfusion in total amounts varying from 400 to 2,250 c.c. was used in 28.8 per cent of the patients.

DR. IRVING F. STEIN.—We have a rather different attitude from Dr. Irving on one or two points, particularly in regard to methods of treatment. In our last five-year series, 1929 to 1933 inclusive, we had no cases of Braxton Hicks version, and we used low cervical cesarean section to the exclusion of the classical section. We use a 10 cm. bag as a preparation for delivery and not for delivery. If one waits for complete dilatation, the operation cannot be placed in the category of accouchement forcé.

At the Cook County Hospital in Chicago we had 55 cases of placenta previa in the last five-year period. Twenty-three were treated by low cervical cesarean section, and in this group there were no deaths. The one death was in a patient with marginal placenta previa who was treated by medical induction. It was a cephalic presentation and forceps were used before there was full dilatation. The cervix was torn and the uterus packed, but the patient died of hemorrhage. This one maternal death gives us a maternal mortality in this series practically the same as Dr. Irving's last five-year series, namely 1.9 per cent. We did no Porro cesarean sections. There were eleven fetal deaths, all prematures. We do not use the size of the fetus as the determining factor. In most of our cases it was a question of the type of previa, the condition of the mother and the amount of hemorrhage.

DR. CHARLES S. BACON.—The question frequently arises when hemorrhage occurs before term whether we should empty the uterus or should carry on the pregnancy for a few weeks to bring the child nearer to maturity. In any case where there is reason to diagnose placenta previa, the patient should be in a hospital, but even then there is a certain danger.

DR. FREDERICK FALLS.—Associated pathology may be of considerable significance in placenta previa. Chronic cervicitis in multiparas with torn cervixes may give rise to puerperal sepsis. The management of placenta previa has frequently to take into serious consideration such complications as toxemia or a heart lesion. We agree with Dr. Irving on the relative frequency of monstrosities.

We have a good deal of respect for the information one can get by a careful rectal examination. If this shows a boggy mass over the internal os and the clinical history is that of simple placenta previa, we have no hesitancy about going ahead with cesarean section or other treatment. We do feel a little safer about doing cesarean sections if no vaginal examination has been done. If, however, a rectal examination is not satisfactory we do not hesitate to do a vaginal examination.

We have not found it necessary to transfuse often. This is probably because our clinic does not accept a large number of cases from the outside. We frequently carry a premature fetus along even after a fairly brisk hemorrhage two or three weeks with the patient in the hospital under control and are always ready to interfere with the slightest recurrence of hemorrhage.

Accouchement forcé is never done in our clinic. We use the Voorhees' bag very seldom. We feel that all cases before cesarean section should be x-rayed if feasible, particularly to determine whether a monstrosity is present. If one is found, we agree with Dr. Irving that delivery should be from below, except in the case of central placenta previa with severe bleeding.

DR. DAVID S. HILLIS.—It is striking that in Boston in 28,000 deliveries there were 1.92 per cent of placenta previa. In the Cook County Hospital, Chicago, in 21,000 deliveries, there was one case of placenta previa in every 352 confinements. That is a discrepancy that is very difficult to explain particularly as the two hospitals are quite similar in their clientele. This difference applies also to premature separation which in Boston occurred once in 96 deliveries and in Chicago once in 524 confinements.

The maternal mortality in Boston in the last five years was 2 per cent, and in Cook County in the same period 4.9 per cent. We had 27 cases of bag induction with one death, 12 cases of Braxton Hicks version with one death from sepsis, 16 cases of cesarean section, low cervical in 11, classical in 4 and Porro in 1, with no deaths.

When section is done in placenta previa it is our practice to make the skin incision low and by palpation through the lower uterine segment try to determine whether

the placenta lies under the anterior wall. If it does, we believe it increases the hazard to the baby and danger of hemorrhage to make the uterine incision through the placental site.

According to our practice when a diagnosis of placenta previa is made, the patient should be brought into the hospital and treated at once. Some twenty years ago I had in a hospital a patient who I felt could be allowed to go on for some time without interference. She was a multipara. She started to hemorrhage, filled a bedpan with blood and died before anyone could reach her.

DR. JOSEPH L. BAER.—Sterile rupture of the membranes should stand in the front rank of treatment for placenta previa. It accounts for the safety of practically every mother for whom it is properly selected, and conserves almost as many worth-while babies as section. It is very difficult furthermore to distinguish between a fetus sufficiently over four pounds to make it worth while saving and one just under four pounds that is not worth the risk of a cesarean section.

I cannot look with favor on a procedure adopted for the safety of the baby that includes an increased hazard to the mother. The mortality in this country from cesarean section varies from 2 to 10 per cent in the best clinics, and we know that cesarean section as it is done with a minimum of obstetric judgment by the general surgeon and in the small community is responsible for a tremendous death rate. I am sure you will agree with me in asking Dr. Irving to modify the advice in regard to cesarean section as given in his paper.

DR. CHARLES E. GALLOWAY.—I have read that low implantation of the placenta predisposes to low marginal insertion of the cord. I myself have had three cases in which the placentas were marginal and the cords came off in the cervical canal. Rupture of the membranes led to prolapse of the cord in one case, and the bag in all three cases killed the baby. Is this a contraindication to the bag?

DR. EDWARD L. CORNELL.—Some of the results of the study by the Maternal Welfare Committee of the city of Chicago indicate that one of the factors which predisposes to a higher maternal mortality is the lack of blood transfusion equipment and facilities in many of the Chicago hospitals. A questionnaire made several months ago indicated that only about 46 per cent of the Chicago hospitals are equipped to give immediate blood transfusion.

Many accidents have occurred because the operator failed to recognize the time the bag passed through the cervix. There is a useful type of Voorhees' bag with ridges running around it which helps to tell the obstetrician the amount of the bag that is out of the cervix.

Dr. Irving did not stress the fact that more blood transfusions should be used in these patients and used early. To give 500 c.c. of blood to a patient who has lost 1,200 to 1,500 c.c. is not enough replacement. We should give large transfusions, anywhere from 1,000 to 1,500 c.c. rather than limit it to a single 500 c.c. transfusion.

DR. HENRY BUXBAUM.—May I ask Dr. Irving how he treats the third stage of labor in placenta previa, if he does a manual removal of the placenta, and whether he packs the uterus routinely after the placenta is delivered?

DR. ALFONS BACON.—The Frontier Nursing Service in Kentucky last spring reported the completion of the first 2,000 deliveries with a total maternal mortality of two cases, both due to heart disease. If the usual incidence held in this group, there should have been 27 placenta previas with no deaths. In that region where transportation is primitive, surgical facilities almost completely lacking, and transfusions are impossible, the conservative type of treatment has been not only necessary but attended with favorable results.

DR. IRVING (closing).—The problem of the woman who has a placenta previa but whose infant has not reached viability is of great interest. Our opinion is that there is no expectant treatment for placenta previa and that once the diagnosis is made the proper treatment is the immediate termination of pregnancy.

The possible etiologic relationship of infection to placenta previa is of great importance. It would be an excellent idea to obtain cultures from the cervixes of all women with placenta previa, to determine if any correlation existed between cervical infection and low placental implantation.

May I call Dr. A. Bacon's attention to the difference between the type of patients delivered by the Frontier Nursing Service and the clientele of a large urban clinic to which many complicated cases are referred by outside physicians. This should explain the difference in frequency of abnormalities.

It is my impression that marginal insertion and prolapse of the cord is distinctly more common in placenta previa than in the case with normally situated placenta.

In cases of placenta previa delivered through the pelvis it is not our policy to extract the placenta manually or routinely to pack the uterus. Both of these procedures are employed only when they are indicated.

FRACTURE OF THE FEMORAL NECK FOLLOWING IRRADIATION

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INTENSIVE study of female generative tract cancer as carried out in our gynecologic clinic has brought to light 14 instances of spontaneous fracture of the femoral neck. Ten cases were found among 471 patients with pelvic malignancy examined in the Gynecological Cancer Conference from July, 1931 to 1934, an incidence of 2.1 per cent. Three additional cases occurred in patients seen prior to July, 1931, and one has appeared since, making in all 14 cases here reported. Ten had carcinoma of the cervix, two carcinoma of the fundus, one carcinoma of the ovary, and one had carcinoma of the vulva.

Fracture was bilateral in 3 cases, occurring at intervals of 10, 13 and 14 months, respectively.

One or two fractures occurring in a large series of patients afflicted with cancer would excite little interest but an incidence of 2.1 per cent appears to be more than incidental.

These patients had been under close scrutiny for several years. Since we lacked satisfactory evidence confirming our impression that we were dealing with spontaneous fractures of the femoral neck of a non neoplastic origin in patients who had received roentgen therapy for pelvic

*Deceased.

malignancy, we purposely avoided reporting them until now. Evidence now available, however, warrants our placing these data before the profession. If these fractures are in some way related to roentgen therapy, and they appear to be, then it becomes desirable in this time of high dosage x-ray therapy to evaluate more carefully the results of such therapy.

Certain general data concerning this group may be of interest. The average age of the group was fifty-seven years. The youngest was forty-two and the oldest seventy-eight years. Thirteen patients are living. One is dead. The latter had an exploratory laparotomy elsewhere about one year after irradiation and died shortly thereafter. Unfortunately no necropsy was performed. In no instance was there history of injury or fall. In every case pain antedated the diagnosis of fracture by months. This was generally located in the hip and radiated down the anterior thigh to the knee. Pain on weightbearing or motion was also noted. An average of seven months elapsed from the onset of hip symptoms until fracture was demonstrated. Roentgenograms of the femurs antedated the diagnosis of fracture by months or years in all but one case. The average time interval from onset of pelvic malignancy to fracture was about three years. (The shortest was nineteen months, and the longest seventy-three months.)

Eight of the 14 patients revealed probable metastatic involvement in the bony pelvis or in the femur uninvolved by fracture, but in no instance was neoplastic growth positively demonstrated roentgenographically at the fracture site. Six patients had no evidence of metastasis at the time of fracture. All patients were reexamined from six weeks to ten months following fracture and all presented unaltered roentgenograms of the fracture site.

Nine patients with fracture had developed fibrous union, sufficient to allow return of partial function. None of the patients, however, showed any callus formation when observed at ten months or later.

Ten of the group received extensive irradiation as shown in Table I, while four received only a small total dose. The latter were in the older age group. Most patients received short wave length roentgen therapy (200 k.v.p., 0.5 mm. Cu.) to four portals around the pelvis, using two anterior oblique fields about 10×15 cm. in size and two similar posterior ports. No direct radiation was given over the femoral necks nor were lateral ports over the trochanters used. Each series consisted of about 200 roentgens (measured in air) applied to each of the four areas every second to fourth day until a total dose of 1,500 to 2,000 r. was reached, usually within thirty to thirty-six days when a definite skin reaction was obtained. Two or three series were given at intervals of three to six months. Radium was employed in eleven cases, the dose averaging 5,000 mg. hr. No definite routine of radium application was considered desirable. Instead, each case was individualized and that treatment out-

lined which appeared best suited to it. Generally, in cancer of the cervix radium was applied as follows: Tandem tubes in the uterine cavity; surface bomb application against the surface of the cervix, screens 1.5 mm. platinum plus 1 mm. rubber; average total dose 5,000 to 6,000 mg. hr., given in twenty-four to thirty hours.

The primary diagnosis of uterine (ovarian or vulval) malignancy was verified by biopsy in all cases.

The skin over the treated area was found to be in perfect condition in six patients. Two showed considerable telangiectasia over the ports. In six patients there was bronzing. In no patient was there any evidence of serious skin damage or ulceration.

TABLE I. SUMMARY OF CASES

NUMBER	AGE	DIAGNOSIS	INTERVAL DIAG. MALIGN. AND FRACTURE	TOTAL EXTERNAL RADIATION	SIDE	DURATION OF FRACTURE	LESSONS OTHER BONES	RADIUM TREATMENT	CONDITION OF SKIN	PRESENT CONDITION
308483	47	Ca. Cervix	19 mo.	14,400 r.	R	22 mo.	Third lumbar	Yes	Normal	Death. No autopsy. Aug., 1934.
303130	56	Ca. Cervix	22 mo.	20,960 r.	L then R	17 mo.	None	Yes	+ Reaction	Living
273164	42	Ca. Cervix	34 mo.	13,640 r.	R then L	20 mo.	Through-out pelvis	Yes	+++ Reaction	Living
295483	58	Pap Ca. Ovary	21 mo.	15,600 r.	R then L	19 mo.	Pelvis	No	+ Reaction	Living
312448	45	Ca. Cervix	33 mo.	17,280 r.	R	12 mo.	Other femur	Yes	+ Reaction	Living
209616	45	Ca. Cervix	52 mo.	7,380 r.	L	35 mo.	None	Yes	± Reaction	Living
150071	53	Ca. Cervix	62 mo.	13,480 r.	L	6 mo.	Left ischium	Yes	Normal	Living
300767	74	Ca. Vulva	31 mo.	3,200 r.	R	9 mo.	None	No	Normal	Living
299590	63	Ca. Cervix	33 mo.	22,560 r.	L	9 mo.	Other femur	Yes	+++ Reaction	Living
326800	68	Ca. Cervix	26 mo.	15,040 r.	L	9 mo.	None	Yes	+ Reaction	Living
304864	50	Ca. Cervix	33 mo.	11,840 r.	R	4 mo.	Other femur	Yes	+ Reaction	Fair
226520	78	Ca. Fundus	73 mo.	8,800 r.	R	6 mo.	Many	Yes	Normal	Critical
276992	62	Ca. Fundus	24 mo.	7,200 r.	R	6 mo.	None	No	Normal	Living
353388	62	Ca. Cervix	32 mo.	11,200 r.	R	2 mo.	None	Yes	Normal	Living

COMMENT

American medical literature contains no reference to this subject, but several foreign articles have been found.

Baensch¹ reports the case of a forty-five-year-old woman with carcinoma of the cervix, proved histologically, who developed spontaneous bilateral fractures of the



Fig. 1.—Case 6. Carcinoma of cervix uteri. Normal appearance of hips at time of radium application.



Fig. 2.—Exactly four years later, showing fracture of neck of left femur.

femoral necks three years after radium and roentgen therapy. He ruled out the usual causes of primary fracture and stated his belief that the bone damage was due to irradiation. Kropp² reports a similar case with fracture of the left femoral neck and comes to the same conclusion. Philipp¹ describes 5 cases with roentgen findings similar to ours, and believes irradiation an important etiologic factor. Again Baensch² reports the case of a sixty-two-year-old woman with an ovarian neoplasm suspiciously malignant who was given postoperative irradiation in the

form of two series of full erythema doses over large ventral, dorsal, and two lateral fields including the trochanters. Eleven months later she developed difficulty with the right leg. One and a half years after the first postoperative series of irradiation the patient fell while walking on a level surface. A spontaneous fracture of the neck of the right femur was found. The skin showed telangiectasia and pigmentation over the regions treated. Skeletal x-rays revealed no evidence of tumor metastases. No tumor erosion was visible, but later a roentgen ulcer was noted over the sacrum.

Almost three years after the fracture was first demonstrated the patient died from a cerebral accident. Autopsy showed sclerosis of the large vessels. *Histologic examination of the area of fracture of the femoral neck showed there were no tumor metastases.* There was pseudarthrosis, rarefaction of the bone substance in this area, replaced by plentiful connective tissue deficient in blood vessels. No tumor metastases were demonstrable—anywhere.

So far as we have been able to ascertain this is the only necropsy study in this type of case. Baensch feels that the large amounts of



Fig. 3.—Nine months later (following plaster cast treatment) evidence indicating union. Pelvis is otherwise normal.

radiant energy applied in this region may later cause damage to blood vessels where nourishment is already poor and weightbearing great. He recommends two convergent ventral and 2 to 3 smaller dorsal fields combined with radium dosages of 5,000 mg. hr.

Additional corroborative evidence is to be found in one of our own cases, Mrs. B., Case 312448, originally admitted with a clinical diagnosis of cancer of the cervix. Treatment consisted of a total of 17,280 r. and radium treatment given elsewhere prior to admission to the University Hospital. About thirty-three months elapsed between probable onset of cervical malignancy and femoral fracture. In the winter of 1934 this patient was seen by our orthopedic surgeon, but operation for ununited fracture of the femoral neck was considered inadvisable when rarefaction of the head and neck of the contralateral femur was noted.

In December, 1935, about one year later, Dr. C. E. Badgley, Professor of Orthopedic Surgery at the University of Michigan Hospital, again saw the patient and

performed Colonna's modification of the Whitman reconstruction operation. The specimen obtained at the time of operation included the femoral head and neck plus surrounding soft tissues and ligamentum teres. Careful microscopic study of the ligamentum teres showed marked sclerosis of the blood vessels, some of which were completely obliterated. Small portions of the synovial surface showed a productive inflammation with a foreign body reaction about fragments of absorbing bone. No carcinoma was seen in sections studied.

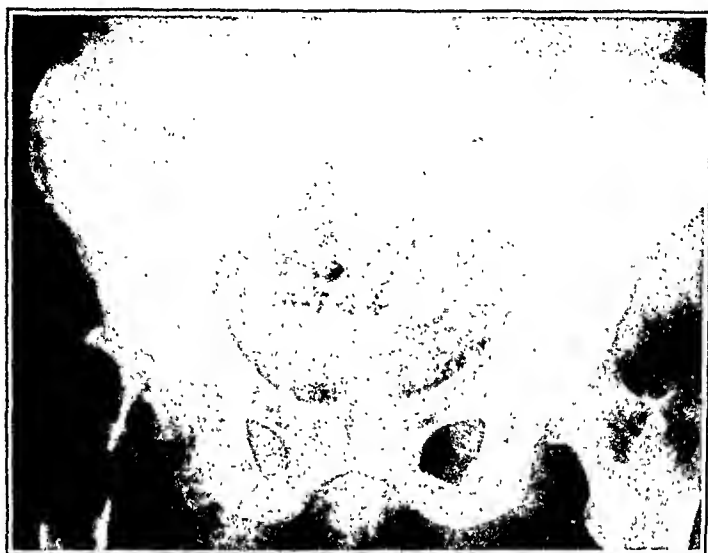


Fig. 4.—Case 4. Carcinoma of the ovary. Fracture of right hip with multiple rarefied areas in pelvic bones.



Fig. 5.—Bilateral fractures demonstrated seven months later.

After decalcification the following changes were noted: Rarefying osteitis, osteoporosis, absorption of bone; foreign body reaction about fragments of necrotic bone in line of fracture; localized new formation of cartilage and bone.

Striking is the fact that these patients appeared to be in relatively good health and the femoral head did not completely disappear but

maintained its calcium content remarkably well. Studies made of the blood in one case showed that calcium and phosphorus content were normal.

The incidence of fracture of the femoral neck in this series is definitely higher than in a comparable group of the general population. Among the general population traumatic fracture of the femoral neck



Fig. 6.—Case 5. Carcinoma of cervix uteri. Fracture of neck of right femur with areas of rarefaction in head and neck of left femur which have not changed in one year. Microscopic examination of fracture site showed no malignancy. (See Figs. 7-11.)



Fig. 7.—Head of femur. Absorption of bone and widening of marrow spaces.

is fairly common after the age of fifty and constitutes about one-third of all fractures at the age of seventy. Spontaneous fracture probably occurs only once or twice in four or five thousand persons of this average age group which is about sixty-five. It is more common in women than in men and may result from relatively minor trauma such as stumbling or turning in bed. The osteoporosis which accompanies age

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seems to be an important etiologic factor. The primary mortality from this injury in ordinary practice is about 16 per cent. The production of callus is unlikely, and the treatment is often operative. Occasionally fibrous union occurs sufficient to permit a partial return of function. Ordinarily the accident is not preceded by symptoms referable to the affected side.



Fig. 8.—Margin of fracture. Bone absorption and callus formation without bone regeneration.



Fig. 9.—Margin of fracture. Higher power of small area of Fig. 8.

Reasons for the phenomena here described are highly speculative. Present-day roentgen treatment of pelvic malignancy employs a higher voltage than formerly. Likewise, the amount, intensity and duration of treatment has increased. Radium, as generally employed, probably has little effect on the femoral neck. Three of our patients received no radium treatment whatsoever.

It is possible that roentgen therapy may, in some way, produce sufficient osteoporosis of the femoral neck to allow spontaneous fracture. Some of our cases appear to exhibit only partial reduction of the blood supply to the head of the femur, as indicated by a bending of the neck and retention of calcium in the femoral head. An obliterative endarteri-

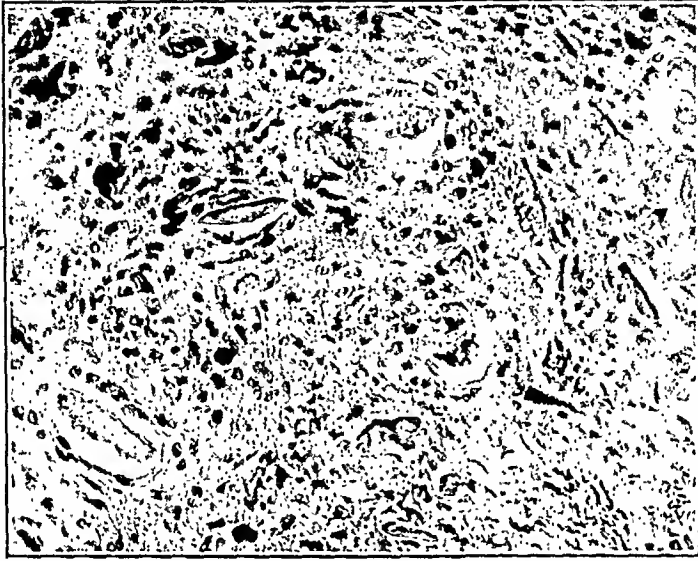


Fig. 10.—Bone absorption. Minute fragments of necrotic bone included in callus at fracture site.

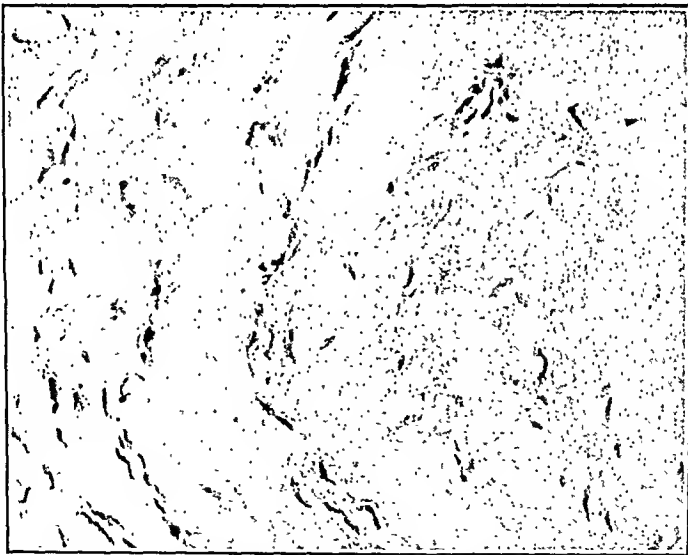


Fig. 11.—Fibrous callus at fracture. Older portions of callus are nearly avascular with dense fibrous tissue formation.

tis in the blood supply to the neck might be a factor, although the obliteration is probably not complete if it exists at all.

Still another possibility is that present-day methods of treatment have prolonged the lives of many of these patients sufficiently to permit development of late skeletal metastases and consequent pathologic fracture.

If our findings are supported by similar cases treated by others, then there is need for a careful evaluation and perhaps for more caution in advancing roentgen dosage.

Additional report (Pathology No. 3690-AN) on bone changes by Dr. John C. Bugher, Assistant Professor of Pathology, University of Michigan. The bone of the entire region shows marked osteoporosis. The trabeculae are narrowed and irregular with a marked increase in the volume of fatty marrow. The density of calcification has been diminished so that the bony structure not only is less substantial quantitatively but also is inferior relatively. In the neck, where this process is most marked, there is a zone of dense connective tissue increase marking the fracture site. Here there is extensive obliterative sclerosis of the nutrient vessels and the callus itself is practically avascular. In the dense connective tissue are found many minute fragments of necrotic absorbing bone. Throughout the fracture region there is an entire lack of osteogenesis; instead, the picture is one of progressive bone absorption and fibrosis.

Jan. 29, 1936, Case 304864 (Table I). Patient died following an injury. Complete autopsy was performed and no residual malignancy was found. The right hip joint was carefully examined and the femoral neck subjected to critical study, the pathologist reporting as follows: "Marked bilateral osteoporosis. Bone absorption with formation of dense callus on right. There is no formation of bone or cartilage in this tissue, the older portions of which present appearances of a simple scar. Marrow completely fatty. On left, there is a younger fibroblastic proliferation with small islands of cartilage and slight new bone formation. Small vessels show progressive obliteration. The appearances are those of an earlier phase of the process as seen on the right."

CONCLUSIONS

1. Fourteen cases of fracture of the femoral neck following pelvic irradiation for gynecologic malignancy are reported.
2. The amount and technic of treatment have varied considerably in this group.
3. Irradiation may be an important factor in producing this complication.
4. The occurrence of this complication does not contraindicate the continued use of radiation therapy in pelvic malignancy, but may call for a revision in the application of such therapy.

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REGIONAL ANESTHESIA IN THE CONDUCT OF LABOR*

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DURING recent years much has been written and much work has been done on the question of relief of pain during labor. It is a subject which is of vital importance to both the obstetrician and patient, but any consideration of this subject must commence with the premise that whatever course is followed, the safety of mother and child is of paramount importance. The relief of pain at the expense of safe obstetrics is not warranted.

The most serious objection to many of our present-day analgesics and anesthetic procedures is the increase in maternal and fetal morbidity and mortality which accompanies their use. The ideal analgesic procedure would be one that would relieve pain entirely without danger to the mother or child. This state of perfection we have not as yet reached, but great strides have been made in that direction so that at present many mothers are given the benefit of a relatively comfortable labor with the assurance that they will come through it all right, and that the infant will not be adversely affected by the drugs which will be used.

This paper is not intended as an exhaustive review of the literature as that has already been done most admirably by Greenhill.¹ Comparatively few references are to be found which deal with the use of regional anesthesia in the conduct of labor; a most surprising fact in view of the popularity of regional anesthesia in surgery today and of its ease of administration and freedom from untoward effects when used for general surgical procedures. The Germans seem to be more familiar with its use in obstetrics than we are; the bulk of the literature on the subject is to be found in the German publications. Recently more references are being made to its use in the American literature, mainly for anesthesia in cesarean section. It would seem that as obstetricians in this country become more familiar with the procedure and the results attendant on its use in the conduct of labor, it will be more widely used and, as in our experience, sought after by the patients. The purpose of this paper is to report our technic and results with the use of infiltration anesthesia in labor in the hope that it may stimulate a more extended use of this valuable procedure.

McCann² in participating in a symposium on the relief of pain in labor has brought out with the help of those men entering into the discussion, the advances

*Read by invitation at the regular meeting of the Honolulu County Medical Society, Honolulu, Hawaii, September 6, 1935.

made in recent years in the relief of pain with the use of various preparations during the first stage, supplemented by nitrous oxide and oxygen during the second stage. They are of the opinion that the first stage can be conducted satisfactorily with morphia and scopolamine or magnesium sulphate or with one of the many barbiturates with or without morphia. These men all favored nitrous oxide for the pains in the second stage, particularly when the head is crowning and as it passes the vaginal introitus. One of the discussors (Bristol)² dwelt on the excessive cost of nitrous oxide, a factor in obstetric analgesia which cannot be lightly dismissed. If given over a period of hours, as is sometimes necessary in long labors, the cost of this inhalation anesthesia is prohibitive for many of the middle class patients. In addition to this purely economic factor, there are many smaller hospitals in which necessity for the constant administration of nitrous oxide with labor pains works a distinct hardship on the staff of anesthetists and in agreement with Risett³ I believe that nitrous oxide should be given only by trained anesthetists if the best results are to be attained.

As stated before, of first importance in determining the type of anesthesia to be used in a given case is the reduction of fetal and maternal morbidity and mortality. It is well recognized and, I think, generally accepted that there is a definite, though small, morbidity and mortality attached to the use of any general anesthetic. Greenhill⁴ has pointed out the disadvantages of inhalation and spinal anesthesia when used on normal individuals and emphasizes the particular necessity for considering these disadvantages on individuals with medical complications.

Of the nine disadvantages mentioned by Greenhill,⁵ some are of particular interest to obstetricians. Patients with toxemias of pregnancy are particularly prone to morbidity, following the use of inhalation anesthetics. Dehydration is undesirable, not only because of its possible rôle in production of ketosis and shock, but its effect on lactation. Gaseous distention is frequently a complication of normal labor as a result of the rapid lessening of the intraperitoneal pressure and anything that augments this uncomfortable complication is undesirable. There is not only a lowered resistance of the peritoneum after inhalation anesthesia, but also of all the tissues of the body, possibly due to the altered tissue reaction, pH, which follows the use of any of the inhalation anesthetics. Postpartum bleeding, or intrapartum bleeding, particularly during the third stage, is encouraged in our experience by the use of any anesthetic agent which is inhaled and absorbed by the blood stream, so that the blood loss of the patient getting a general anesthetic is somewhat more than of the patient who gets no anesthetic.

On the other hand, there are a few disadvantages to local infiltration or nerve block anesthesia: (1) It cannot be used in the presence of infection, (2) the busy practitioner may not arrive in time to inject

the anesthetic, and last (3) there are a few patients who are so emotionally unstable that they become very unruly unless rendered unconscious. The first of these disadvantages, of course, cannot be overcome, infected tissues should never be invaded by an agent which is likely to spread the infection. The second objection is mentioned only to be answered. The obstetrician should make every effort to arrive at the delivery in time to inject the anesthetic agent. The third disadvantage may be partially met by proper preparation of the patient during the first stage of labor and by establishing the proper rapport between obstetrician and patient from the time of the first prenatal visit. If such rapport has been properly established, the last objection will be found tenable in only a small number of cases. It has in fact been our experience that patients have almost unanimously preferred local block to inhalation anesthesia, this being particularly true of multiparas who have had the opportunity of comparing the two forms of anesthesia.

To enumerate briefly the advantages of local infiltration or block anesthesia: It is easy to administer, safe from a standpoint of maternal and fetal morbidity, gives almost complete freedom from pain during the late second stage and actual birth of the baby, relaxes the muscles of the pelvic floor to such an extent that multiple small lacerations are reduced to a minimum, allows episiotomy, forceps operations including such procedures as the Scanzoni maneuver, manual rotation of the posteriorly presenting head, and repair of the episiotomy wound. The immediate appearance and condition of the parturient woman, following delivery by this method in contrast to her appearance and condition following inhalation anesthesia, are so striking as to leave few doubts in the mind of the obstetrician as to the relative merits of the two procedures. The use of local infiltration or block anesthesia allows one to perform practically all the obstetric operations without resorting to inhalation anesthesia with its disadvantages noted above.

In 1930 Torland,⁴ citing the work of Braun, and Gellhorn, who in 1913 advocated the use of perineal anesthesia in obstetrics, stimulated us to test its efficacy. During the early months of our work cases were selected (for various reasons) which were thought to be well adapted to the method, main considerations being multiparity and the stoicism of the Nordic heredity. The results in these selected cases were so satisfactory that the procedure was extended to all classes of cases, and in only a few was it found necessary to resort to inhalation anesthesia. In many of these earlier cases good anesthesia was not at first obtained but as our technique improved we got fewer failures, and it has been some time since any patient has complained from lack of good anesthesia. This report deals with a group of one hundred consecutive cases selected at random in which

delivery was accomplished by regional block and infiltration anesthesia and in which no inhalation anesthesia has been used. No attempt has been made to select normal or easy labors.

METHOD

The technic of administration is a combination of that advocated by Tarland⁴ and King which is a combination of nerve block and infiltration. The instruments necessary consist of a Luer Lok syringe of 10 c.c. capacity, two local anesthetic needles, of about 19 gauge, a medicine glass and novocaine or procaine 1 per cent solution, 40 c.c. With the patient in the lithotomy position, the skin of the perineum and vulva is prepared by scrubbing with neutral soap and water and douched off with either a weak iodine solution or merthiolate solution. No other antiseptic solutions or applications are used, reliance is placed in thorough use of soap and water. Before the patient is draped the surgeon puts on a pair of sterile gloves which are used for the administration of the local anesthetic, and then he changes for a fresh pair for the delivery. At a point 2 cm. above the posterior border of the vaginal outlet and 2 cm. medial to the pubic ramus, the needle attached to a syringe containing 1 per cent procaine solution is inserted until it pierces the fascia at a depth of about 3 to 4 cm. The piercing of Colles fascia transmits about the same sensation to the operator as does the piercing of the arachnoid in performing arachnoid block. In this situation 5 c.c. of anesthetic solution are injected. The same procedure is carried out on the opposite side. This injection serves to block the filers of the pudic nerve which supply the skin over that area and also the labia and clitoris. There is also some blocking of the fibers of the genitocrural which supplies this same area and are to be found at the same level under Colles fascia. At a point midway between the ischial tuberosities and the anus the needle is again inserted at an angle so that the point of the needle impinges on the tuberosity. It is then withdrawn a short distance and reintroduced about 1 cm. medial and about 2 cm. deep to the tuberosity. At this point 10 c.c. of 1 per cent procaine are introduced, the last 3 or 4 c.c. being introduced after the needle has been withdrawn 1 or 2 cm. A like injection is carried out on the opposite side, this injection serving to block the larger branches of the inferior pudic nerve as it emerges from behind the gluteus muscle. These nerve branches are the superior perineal, inferior hemorrhoidal, and dorsal nerve to the clitoris, all of which branch from the inferior pudic in this region and lie in the plane just deep to the ischial tuberosity and between it and the anus. Inasmuch as our operative activity is concentrated in the perineum due to the fact that, unless contraindicated, we do routinely a medium episiotomy, about 10 c.c. of procaine are infiltrated into the perineum in the median line and well into the vaginal mucosa. In a short time, usually about five minutes, anesthesia is effective so that the patients usually state they feel numb and have lost the grueling pain which accompanies the attempts at expulsion with the fetal head on or near the pelvic floor. In the great majority of cases, good anesthesia is evidenced by relaxation of the pelvic floor and loss of pain, although tactile sensation is not altogether abolished. With the onset of good anesthesia any necessary procedure for the delivery of the baby may be carried out. Episiotomy and repair, manual rotation of the persistent occipitoposterior head, Scanzoni maneuver, and all of the low and midforceps deliveries have been satisfactorily performed under this anesthesia.

DISCUSSION

It will be seen from the tables that all the cases did not fall into the classification of normal labor. It is true that there are no very serious complications, such as placenta previa, marked disproportion, etc., in

this series. Such cases would be handled when there was an absolute indication by low cesarean section and are not included in this series. Only those patients not delivered from below are excluded from this series of 100 consecutive labors. By the use of the Thom technic of pelvic roentgenography together with careful clinical examinations, we usually segregate our cases for section prior to the onset of labor and, therefore, do not have in this series any patients who required a test labor. The incidence of cesarean section is 0.19 per cent of this group of 100 cases, inasmuch as we started with 102 cases and dropped the two sections, one of which was done for disproportion with vertex presenting and the other for disproportion with breech presenting.

Of the foregoing cases, 14 can be classed as abnormal, as their labors did not conform to the normal, either due to abnormal presentation of the fetus or due to some maternal influence which either prolonged the labor or placed it in the class of a pathologic labor. This is an incidence of 14 per cent abnormal labors. It will be noted that low forceps were used often. This procedure is very frequent in primiparas, as we feel we can definitely shorten their labors with no increase in fetal or maternal morbidity if forceps are properly used. Manual rotation of the head is the procedure of choice in occipitoposterior positions, the Scanzoni maneuver occurred only twice, once in a rather large baby with a persistent occipitoposterior position which could not be rotated manually, the other in a patient with narrow transverse diameter in which the head would not rotate. In these cases application of the forceps, rotation of the head, and reapplication of the forceps with delivery were accomplished without pain or trauma to the mother and with no apparent effect on the infant. This in spite of the fact that relaxation of the uterus has been deemed necessary in the past in order to effect rotation to the occipitoanterior position. Follow-up on these two patients shows an excellent result ten months postpartum with healthy infants gaining weight normally. It is felt that a Scanzoni maneuver is much less dangerous to a patient anesthetized locally than one under deep anesthesia, as it makes careful application and manipulation of the forceps mandatory. This holds true for all of the operations attempted during labor, particularly to the application of forceps and constitutes one of the chief advantages to the use of local anesthesia.

In none of the cases reviewed was inhalation anesthesia necessary. All patients were questioned immediately after delivery and at intervals thereafter to determine their reaction to the use of this type of anesthesia. Most of them stated that they did not have pain when the baby was born and only 3 or 4 knew that they had had forceps applied. With our present analgesic methods, many of the patients have no memory of the labor. Breech deliveries offered no special problems. We have not resorted to version and extraction in this

series, so that no facts are available in this class of case, but in view of the ease with which the Scanzoni maneuver and manual rotation are carried out, it is felt that version could probably be performed under this same anesthesia.

TABLE I. PARITY

PARITY	PER CENT
Primiparas	46
Multiparas	54

TABLE II. POSITION

POSITION	
Occipitoanterior	87
Occipitoposterior	12
Breech	1

TABLE III. TYPE OF DELIVERY

TYPE OF DELIVERY	
Episiotomy, repair	50
Low forceps	27
Midforceps	2
Extraction	1
Manual rotation	5
Scanzoni	2
Spontaneous rotation	4
Spontaneous delivery	47

In the last 100 consecutive labors, cesarean section excluded, all the patients were delivered relatively painlessly by using the following technic in the conduct of their labors. The first stage was conducted with the use of one of the barbiturates augmented by small doses of morphine and hyoecine. For the average patient sodium-iso-amytal (pentobarbital) is used, the initial dose being 0.29 gm. given as soon as the contractions become well established and the patients begin to complain of dilating pains. This drug is then repeated in one-half an hour with about 0.19 gm. more or less, depending on the size of the patient and length of labor. One-half to one hour later morphine sulphate and hyoscine are given in doses of 0.016 to 0.008 of morphine sulphate and hyoscine 0.00045. We try to give the morphine sulphate at least two hours before the expected time of delivery. Contrary to experience of Irvine⁵ and others and if given in small doses, the morphine apparently does not become a serious respiratory depressant. It materially aids in quieting the restlessness which accompanies approximately 16 per cent of labors conducted under pentobarbital and scopolamine and overcomes the big objection to the use of this combination of analgesics for amnesia. When the cervix is completely dilated the bag of waters is ruptured artificially with an amniotome if it has not already done so spontaneously. Descent of the head is then usually rapid, except in those labors complicated by abnormal presentations or other factors, in which case complications must be handled as they arise. In any event, at about this stage, the patient is prepared by scrubbing the perineum and vulva with neutral soap

followed by douching the external parts with weak iodine solution or merthiolate, and the local anesthetic is injected according to the method described. Delivery then takes place or the necessary operative procedure is carried out to place the fetus in the normal position, so that delivery may be accomplished. It has been found that most situations encountered during delivery from below can be met and labor terminated under a combination of local block and infiltration anesthesia with pentobarbital, morphine, and scopolamine during the first stage of labor. Fetal and maternal morbidity and mortality are reduced to a minimum (Tables IV, V, VI). It is felt that this type of anesthesia is far superior to inhalation anesthesia in the conduct of labor, be it normal or complicated, primarily because in addition to producing good analgesic and anesthetic results it demands respect for tissues and requires the careful handling of both tissues and instruments.

TABLE IV. MATERNAL MORBIDITY

CAUSE	PER CENT
Phlebitis, obese woman (weight 247 pounds)	1
Premature separation placenta	1
Deaths	0
Infections	0

TABLE V. FETAL MORBIDITY

DIAGNOSIS	PER CENT	REMARKS
Congenital hypertrophic		Ramstedt operation at
Pyloric stenosis	1	14 days. Recovered.
Cleft palate	1	Operated. Recovered.

TABLE VI. FETAL MORTALITY

DIAGNOSIS	PER CENT	
Prematurity, 5 months	1	Stillborn.
Spina bifida, complete	1	Stillborn.
Congenital polycystic kidneys	1	Died 7 days postpartum, 3 days after right nephrectomy, left kid- ney also polycystic.

TABLE VII

	PER CENT
Operative deliveries, total	53
Spontaneous deliveries, total	47
Required operative delivery	14
Elective operative delivery (episiotomy, low forceps)	36

CONCLUSIONS

1. Local block and infiltration anesthesia have a wide application in obstetrics in the conduct of labor.

2. Most labors can be conducted and successfully terminated with a minimum of pain, low morbidity and mortality by the use of the type of anesthesia and analgesia described. Many patients so handled do not remember the labor or delivery.

3. Abnormal presentations and labors can be successfully conducted with this type of anesthesia.

4. Episiotomy and repair can be accomplished with the same anesthesia as that used for the delivery.

5. Although no definite statistics are available at present, it is our impression that blood loss during and after the third stage is much reduced with regional anesthesia.

6. In addition to producing a relatively painless labor and delivery regional anesthesia demands careful handling of instruments and respect for tissues which ultimately reduce morbidity and mortality in both mother and infant and, therefore, constitutes one of the major advantages to the use of this method.

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ANTEPARTUM FETAL DEATH*

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THE subject of antepartum fetal death carries us through so many ramifications that no one part can be treated more than superficially in the time permitted for this paper. My text is the result of a review of some of my own work combined with that of cases from the Obstetrical and Gynecological Services at Cook County Hospital. I am indebted to them and to the Record Library of that institution for courtesies in supplying the many histories for this review.

When an obstetrician attempts to induce labor near term, because of a dead fetus which is erroneously supposed to be in the uterus, or a gynecologist removes a uterus for a presumed soft fibroid, which turns out to be a missed abortion, he has misinterpreted or neglected evidence which, though hidden, was present and available. The pitfall he has fallen into is usually so concealed that others with far greater experience and ability have difficulty in avoiding similar fates. The location of the pregnancy, whether within the uterus or outside of it, is also a part of this available evidence and, important as it always is, it is secondary to the problem considered here. Clinically the diagnosis of simple pregnancy is

*Read at a meeting of the Chicago Gynecological Society, November 15, 1935.

not always simple. The determination of life or death of the ovum is important and is reflected in the type of treatment pursued. I shall take up only some of the practical features involved.

For purposes of study, I have divided antepartum fetal deaths, which may occur from the moment of conception to term, into two groups: first, those which occur before quickening, and second, those which occur from quickening to term. In uterine pregnancy the products of conception, when dead, are usually expelled before a diagnosis is possible, but they may be retained until all of the original symptoms are forgotten, even as long as sixty years.

When the dead embryo or fetus is neither in the uterus nor tube, but in the abdomen, the findings may be so eluded that our every faculty is inadequate for correct diagnosis. When the question of death is confounded by the presence of infection, by various types of degenerative processes, by the death of only one fetus in a multiple pregnancy, and other conditions too numerous to mention, the train of symptoms becomes so distorted that the establishment of a typical syndrome of death is impossible.

a. *Before Quickening*.—The diagnosis of pregnancy should ordinarily precede any attempts to diagnose embryonic death. Of importance for this are the usual symptoms: amenorrhea, nausea and vomiting, fullness of the breasts, etc. The palpable tumor mass whether in the uterus or tube is often, in the very early stages, negligible to touch. If, in a woman of childbearing age, the uterus or tube is found to be enlarged, and the above list of symptoms are obtained, one can usually make a positive diagnosis of pregnancy. The Asehlheim-Zondek test alone may be sufficient for that. But when these subjective and objective symptoms, at a subsequent visit of the patient, disappear or change, then only should one suspect fetal death. Roentgenography reveals nothing during this stage. If the patient is seen for the first time after these changes have occurred, and the pregnancy test is negative, the difficulty is even greater. There are, then, no objective comparisons and the list of subjective symptoms may be influenced by time and may, therefore, become unreliable. When spotting, extensive bleeding, or symptoms of internal bleeding and peritoneal irritation exist during pregnancy, the diagnosis is chiefly concerned with its location and fate rather than with its life or death.

The term "threatened uterine abortion" applies to attempts on the part of the uterus to expel the products of conception. So the term "threatened tubal abortion" may similarly apply to tubal pregnancy about to be expelled into the abdominal cavity. In neither case is the death of the embryo implied. At this stage even establishment of the diagnosis of pregnancy and its location is, without exploration, often a big undertaking, but add to this the diagnosis of life or death of the embryo, and it becomes a real accomplishment. The change from a

positive to a negative Aschheim-Zondek is most significant. However, a positive pregnancy test is often present for a week or more after death, and thereby, for a time, adds to the difficulties already existing.

In uterine threatened abortion, which progresses to complete abortion, the question is relatively unimportant because the materials for diagnosis are at hand. In the one in which bleeding stops, time will reveal if the uterus keeps growing, and if so at what rate. With a missed abortion in the uterus or with the development of a mole, that organ usually remains stationary in size. It may even get smaller. Rarely, it gets larger. If the uterus grows as it does in a normal pregnancy, difficulties may again be encountered.

As an illustration of such growth I present: Mrs. F., para iii, a rather stout woman who was confined by me two years previously, came to arrange for another confinement. There was amenorrhea for three months with only a slight nausea, no vomiting. Because of a thick panniculus and a very deep pelvis, I was unable to outline the uterus. Two months later she inquired about not feeling the baby move. This time the uterus appeared about level with the navel, no heart tones were audible. At the sixth and seventh months the uterus was at the proper levels for the period of amenorrhea. No ballottement; and no heart tones were audible. There was some dyspnea on exertion. Nothing wrong was suspected even though heart tones were not heard. This was a common failing in those days and still is. Shortly before the calculated term date she complained of spotting and intermittent pains and was advised to go to the hospital. Only when a grapelike mass came away during a vaginal examination was the diagnosis made. I was dealing with a hydatid mole for six months before it was recognized. The normal rate of growth and absence of suspicious symptoms led me to believe I was dealing with a normal case. At the patient's first visit, I had overlooked a missed abortion which had undergone this type of degeneration.

When there are symptoms of internal bleeding in a suspected tubal pregnancy, the diagnosis of "threatened tubal abortion" or "threatened tubal rupture" can be made by a keen diagnostician even before actual rupture. If there is no interference and the internal bleeding shows evidence of having ceased, as so often occurs, and in the course of a few days there is no growth of the tubal mass, one might, as in the case of uterine pregnancy, make the diagnosis of a "missed tubal abortion." With an increasing firmness of the tubal mass, subsidence in pain and discontinued internal bleeding, even a "tubal mole" may be diagnosed. These conditions parallel those of death in the uterus.

From a study of many extrauterine pregnancies which historically showed the exact time of rupture as from two weeks to three months before operation, I noted that where the pathologic report is given as "old tubal pregnancy," death of the embryo, with some form of degeneration, was implied. Operation was indicated because of pain alone in 100 per cent of the cases. Constitutional symptoms like those listed by DeLee, Litzenberg, and others, for missed abortion or intrauterine death, namely, malaise, anorexia, headache, loss of weight, chilliness, tachycardia, foul taste, bearing-down sensation, and increasing invalidism,

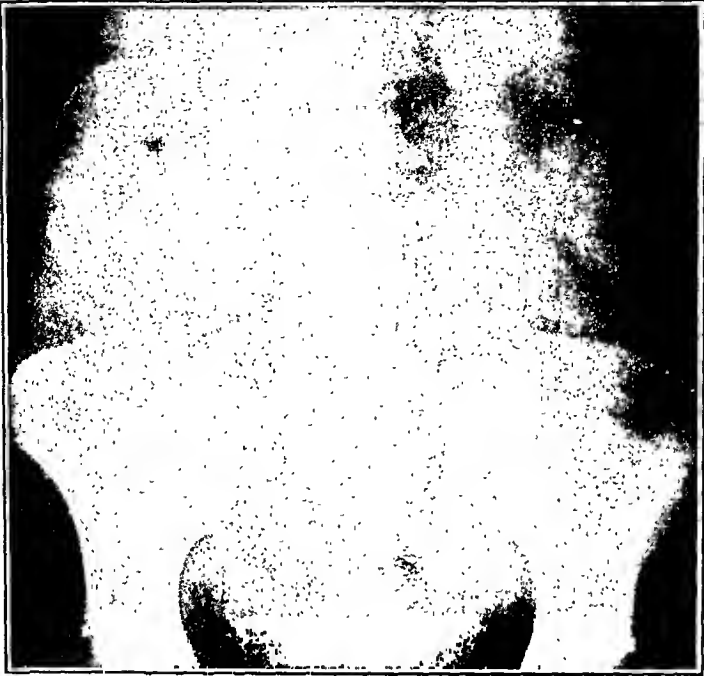


Fig. 1.



Fig. 2.

Figs. 1 and 2.—Showing two stages of overlapping encountered in a breech presentation, the interval being ten days.

were not present. Only in rare instances a few of these symptoms were found and then only in the presence of infection. Even in the cases of *intrauterine* deaths studied, such a list of symptoms was a rare exception rather than the rule. Constitutional symptoms traceable to the death alone were conspicuously absent. I cannot explain the reason for such a discrepancy in symptoms unless absorption from the degenerating products of conception, in this group of cases, was relatively insignificant. The symptoms listed by these authors should apply with equal force in all cases regardless of location, if fetal death exists for more than a few days. With the exception of the more rapidly growing hydatid mole,



Fig. 3.—An early pregnancy a few days after cessation of movements.

failure of growth of the uterus or tube after a positive diagnosis of pregnancy was the only constant symptom. Negative pregnancy tests alone are unreliable.

b. *From Quickening to Term.*—Abortion or rupture of a tubal pregnancy into the abdominal cavity is common and immediate operation after diagnosis is the rule when diagnosed. However, there are many individuals alive today who could never have been born without a violation of this rule. Continued growth of a uterine or of an abdominal pregnancy readily becomes apparent if life exists. In the latter cases it may be the mother's only opportunity to conceive, so diagnosis need not necessarily

mean laparotomy. Only when septic symptoms from an abscess, or symptoms of internal hemorrhage, are so severe that her life is endangered, is hurried laparotomy advisable. Even when death of the fetus occurs, prompt laparotomy is not essential: delayed operation may be much simpler and far safer to the mother. A case with which I am familiar, reported from Dubuque, bears this out. An abdominal pregnancy went to term and because of the illness of the original attendant, was not operated upon. The fetus died in the abdomen and about two years later, a pelvic mass the size of a small grapefruit was removed. To remove this mass it was necessary to sever only a small pedicle. A rather formidable operation became simple in the intervening two years. The



Fig. 4.—A later pregnancy shown four days, at most, after cessation of movements and heart tones.

mass removed in this case contained the collection of fetal bones belonging to a fetus originally shown by x-ray to be at term. Attempts at delivery from below had been made on several unsuccessful occasions, without the diagnosis of the location of pregnancy in the abdominal cavity being made. Fortunately this line of treatment was discontinued.

After the second half of pregnancy begins, fetal movement may be felt, and heart tones may be heard. Sufficient calcium has been deposited even at quickening to show the fetus clearly by x-ray. Each month thereafter the increased deposit of lime adds greatly to details which can be brought out in the film.

The feeling of fetal movements by patients and the hearing of fetal heart tones by attendants are just as variable as the concerned individuals

themselves. One patient may feel them early, late, or not at all. I have been able to palpate them unmistakably myself, and even have seen vigorous fetal movements without the patients being aware of their presence. But when once felt by the patient, her statement that they have ceased and have not been felt since is of utmost importance until the contrary is proved. In most cases which I have attended in private practice, the patient has suspected fetal death before I could make the diagnosis. But in clinics it is not unusual to discover the death before the patient is aware that something is wrong.

Early in this stage one man may hear fetal heart tones long before another. I can locate them sooner and hear them better in the hospital than in my office, and better with one stethoscope than I can with another. The absence of fetal heart tones when they have once been heard is not as important a criterion of fetal death as the matter of movements. Hydramnios may obliterate both completely, the heart tones being lost first. There is, however, another sign associated with this absence of fetal heart tones which to me is of greater value than the lost heart tones themselves. It is the peculiar indescribable silence over the entire uterus which heretofore has had a distinctive sound of its own, independent of fetal heart tones, fetal souffle, uterine bruit, or other noises. You have all probably noted it in cases of fetal death; I have never seen it mentioned in print, so I call it to your attention and emphasize it as a silence that can truly be "heard." I have noted this silence as early as the fifth month and have come to consider it still another important diagnostic sign and worth checking.

Little reliance can be placed on the amelioration of any disagreeable pregnancy symptoms, such as nausea and vomiting, which as a rule have stopped by this time. The improvement in toxemias, if any, and the reduction in hypertension without toxemias are likewise not trustworthy. Stationary or improper rate of growth of the uterus and crepitation of the skull bones are more reliable. The list of symptoms of missed abortion mentioned before does not apply in this stage either. Was it passed along from one generation of authors to another without question like so many other things in medicine taken at face value?

Most obstetricians, even though some are still skeptical of its value, today depend on roentgenography for final confirmation of their diagnosis before attempting treatment.

In my inaugural thesis before this society in December, 1921, I brought out the fact that "over-riding of the skull bones with cephalic asymmetry are signs of fetal death." Since then, there has been a world-wide investigation of this statement with the accumulation of a rather voluminous literature on the subject. There are papers which confirm, refute, and supplement what I presented before you at that time, but the fact nevertheless remains, that overlapping of the skull bones is still the last word in the establishment of roentgen diagnosis of antepartum fetal death.

When it is important to make the diagnosis early and it is impractical to wait to establish a discrepancy between size and period of gestation, this overlapping is the earliest reliable evidence and may be observed as early as four days after death. This sign is present in all cases of fetal death where sufficient ossification exists in the skull to form at least a semirigid casing for the brain. It appears sooner or later, the degree depending on the interval between death and roentgenography. I have never seen it in the living fetus before the onset of labor (Stein and Arens to the contrary notwithstanding). Lightening usually occurs without labor pains but occasionally "false labor" may be necessary to bring about the molding required for the head to enter the pelvis and so the overlapping *may* become visible before the onset of true labor pains.

It is well recognized that brain tissue is the first to show postmortem degenerative changes. Therefore, it is reasonable to assume and we have many instances at autopsy of the newborn to prove it, that skull collapse is the result of brain collapse and is the first skeletal change in the fetus which should be noticed after death. After the onset of labor the sign has no value. And, of course, after labor its significance is not obstetric. During pregnancy this change as shown by roentgenography, together with "audible" silence over the abdomen and the negative Aschheim-Zondek, make a conclusive, objective triad of symptoms which, after quickening, are indicative of antepartum fetal death.

DISCUSSION

DR. WILLIAM J. DIECKMANN.—There have been a number of reports in the literature that in cases of missed abortion, death of the fetus in utero and extrauterine pregnancy going to term, there is a toxic manifestation on the part of the mother, such as temperature or the development of acidosis or ketosis. I have not seen any of these if the patients have not been examined or otherwise manipulated. I would like to ask Dr. Horner if he has noted any toxic manifestations such as these to which we could attach significance, excluding the psychic manifestations that the mother might have.

DR. FRED H. FALLS.—Occasionally we have been told by a roentgenologist that the overlapping of the skull bones of a fetus found on the x-ray film meant that the baby was dead, when very obviously from the clinical findings the fetus was alive. One should be very careful to go through with the obstetric examination as well and not accept the x-ray findings, unless they agree with the clinical findings.

Some years ago I described an instrument, the vaginal stethoscope, which I used in determining death of the fetus in utero between the fourth and fifth month.

This is like an ordinary stethoscope, except that the barrel or portion between the bell and the end to which the ear pieces are attached is approximately six inches long. This permits the application of the bell to the anterior vaginal wall above the cervix so that fetal heart tones and fetal movement, if present, can be clearly heard through the lower part of the anterior uterine wall.

DR. GEORGE H. REZEK.—Using the Schneider modification of the Aschheim-Zondek test, we have found, with the fetus living, the typical positive reaction.

in that the follicles were hemorrhagic throughout. When the fetus was dead, we found a reaction characterized by hemorrhage around the periphery of the follicle, which we termed the dead fetus reaction. The cause of this change has not been determined, but we found that in 70 out of 73 cases where we obtained this dead fetus reaction, a macerated fetus was expelled sometime later. Contrary to what has been reported, we have never obtained a negative Schneider test where we had a dead fetus in utero even though twenty-eight days had elapsed since the last hearing of fetal heart tones. This reaction has been obtained as early as twenty-four hours after the last hearing of fetal heart tones.

When a diagnosis of dead fetus in utero was made by the above tests, other tests were run every three or four days until the fetus was expelled and one was run twenty-four to forty-eight hours after expulsion of the fetus. While the fetus was retained in utero, we always got the dead fetus reaction, and twenty-four hours after the expulsion of the dead fetus, the test was negative.

We have had three false reactions. In two the fetus was alive and the Schneider modification of the Aschheim-Zondek several days later revealed a positive reaction. In the third case the patient was lactating, but not pregnant. One must be careful to distinguish between the reaction that one gets with a lactating woman where one has a peri-follicular hemorrhage and not hemorrhage about the periphery of the follicle. Tate has reported a series of seven cases with five accurate diagnoses, and Jeffcoate of England has a series of nine with seven accurate diagnoses.

DR. HORNER (closing).—It is remarkable that in this large series of about 200 cases, which I studied, there were none with symptoms attributable to intoxication from the dead fetus. The patients came to the hospital only because they had pain. It is not unusual to have patients come to the office for their usual routine of prenatal examination without symptoms, although fetal heart tones are absent and fetal movements have ceased. Fetal death is often suspected first by the mother, only because of the absence of fetal movements and not because of symptoms later attributed to absorption.

Dr. Falls' instrument is a clever device, more applicable in those cases where the fetus is alive. When the heart tones are absent at one examination, they may be heard later when the back has swung closer to the instrument. I question whether the auscultation of fetal movements can be positively obtained any earlier by vagina than by the abdominal route.

Weber, E.: Sodium Evipan in Obstetrics and Gynecology, *Rev. franç. de gynéc. et d'obst.* 29: 1071, 1934.

Weber recommends the use of sodium evipan anesthesia in obstetrics and gynecology. It possesses the following advantages: Simplicity of administration, rapidity of effect, psychic control of the patient, absence of a period of excitation at the beginning of the narcosis and upon regaining consciousness, absence of salivation and of hypersecretion of the respiratory organs and rarity of postnarcotic inconveniences such as vomiting and headaches. Evipan appears to be an ideal drug for short operative procedures. In obstetrics it is particularly useful during labor but only when delivery is imminent, and cannot be used for the purpose of obstetric analgesia.

J. P. GREENHILL.

FURTHER IMPROVEMENT IN PELVIMETRIC ROENTGENOGRAPHY*

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(From the Department of Obstetrics, Georgetown University School of Medicine)

IN PREVIOUS communications my technic and the merits of antero-posterior¹ and lateral roentgenography² have been described. It has been shown that the former procedure, although more complicated than that which is practiced generally, may be proved accurate within two millimeters in contradistinction to the work of other authors who seem to regard very lightly an error as great as a centimeter or more. It shall also be shown that the simple lateral technic originally proposed maintains a similar degree of accuracy.

ANTEROPOSTERIOR ROENTGENOGRAPHY

To permit intelligent discussion of the new improvements, a brief review of the work referred to is in order. With the use of my obstetric inclinometer,³ the height and inclination of the symphysis are measured (Fig. 1, *A*). The length and inclination of the diagonal conjugate are also noted (Fig. 1, *B*). A pelvigram is drawn by taking any point on a horizontal line and laying off the height and inclination of the symphysis as well as the length and inclination of the diagonal conjugate. The symphysis and sacrum are sketched in. A line is drawn from the upper border of the symphysis to the sacral promontory, representing the true conjugate (Fig. 2). A protractor, placed at its intersection with the horizon, measures the inclination of the inlet or of the pelvis (Fig. 2). The length of the true conjugate may be accurately measured with a centimeter scale, or its length may be determined without the use of pencil and paper, by merely constructing the obstetric triangle with the calculator incorporated in the inclinometer.^{3, 4} Also, the inclination of the inlet may be determined directly with the calculator and protractor, as described in a previous paper.¹

Having determined the inclination of the pelvis, the film is supported close to and beneath the patient's buttocks, in a plane parallel to the inlet. The x-ray tube is placed over the approximate middle of the inlet, so that its center ray will strike perpendicularly. Exposure is made, but before the film is developed, or any apparatus removed, the distance from the target to the film and the target to the inlet must be known (Fig. 3). The cassette containing the exposed film is then placed directly beneath an x-ray tube at the tube to film distance, and a lead plate with perforations 1 cm. apart throughout its surface is interposed parallel to the film at the tube to inlet distance (Fig. 4). When a flash exposure is now made, the holes in the lead plate will produce dots on the film, and the distances between them will be identical with the degree of enlargement that the inlet encounters in being transferred to the film. Thus the anteroposterior or transverse of the inlet is measured by counting the dots on the developed film (Fig. 4).

*Read at a meeting of the Washington Gynecological Society, November 23, 1935.

The inclination of the pelvis varies in different women, a fact which Garnett and I have elaborated upon in a paper pertaining to that subject. Suffice it to say, that in a series of carefully selected and personally studied cases it varied between 70 degrees and 7 degrees. The average inclination in the recumbent posture, I found to be 42 degrees. In the standing posture it was 48 degrees. In order to obtain accurate pelvimetric roentgenograms, the inclination of the inlet must always be known, so that the film may be parallel to the inlet and the tube perpendicular to the middle of the inlet. Otherwise the image is unequally distorted and measurements are not dependable,¹ a factor of great importance in the study of borderline pelvises.

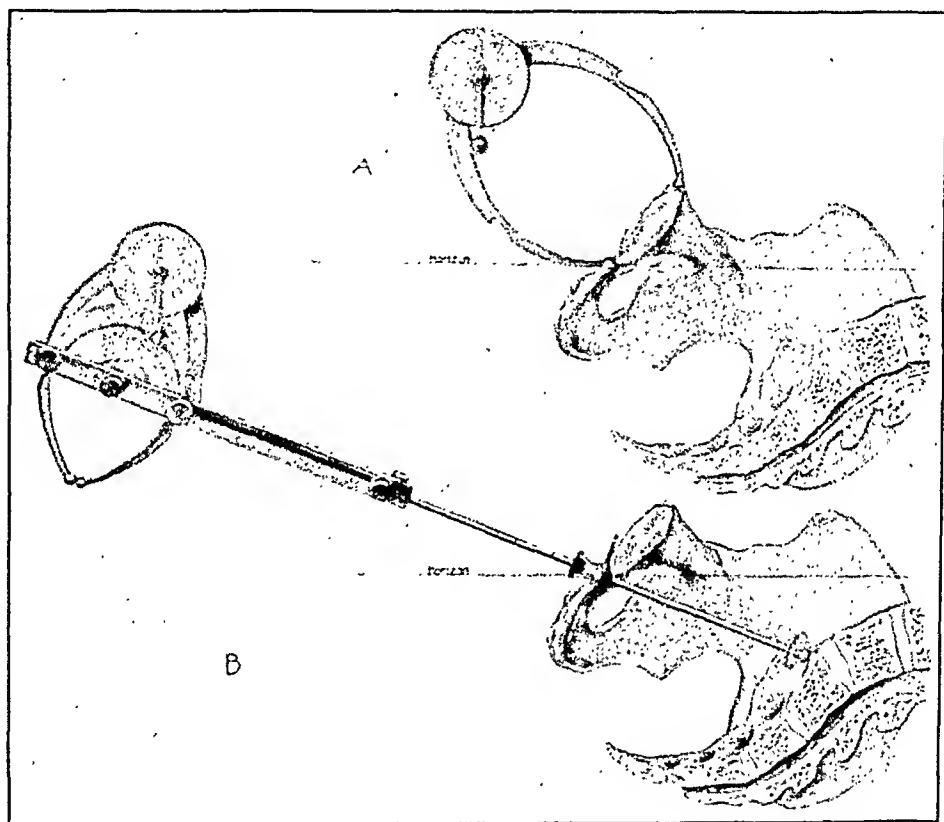


Fig. 1.—A, Measuring height and inclination of symphysis with the caliper or author's obstetric inclinometer. The pendulum denotes inclination, while the indicator on posterior surface of caliper denotes distance. B, The assembled inclinometer measures the length and inclination of the diagonal conjugate. Length recorded on the graduated rod; inclination recorded by the displacement of pendulum on face of caliper.

In the anteroposterior technique¹ originally proposed, the patient's legs were placed in the lithotomy position (Fig. 3). Flexing the legs on the abdomen increases the inclination of the inlet, and where this plane approaches the perpendicular to the spinal column, an x-ray tube to be placed so its center ray will pierce the middle of the inlet (Fig. 3) will not only come to occupy a position dangerously close to the patient's chest and face, but the rays will be directed through the entire length of the uterus and its contents, resulting in a very faint image which will be of little or no value.

To overcome these objections, I measure all patients in the recumbent posture. As shown in the illustration (Fig. 5), the buttocks are brought to the edge of an ordinary examining table and the separated thighs are supported on two plain wooden tables, which are about two inches higher than the one upon which the patient rests, thus allowing for the recess below the buttocks, and putting the spinal column, pelvis, and legs in the relationship they would occupy were the patient standing.

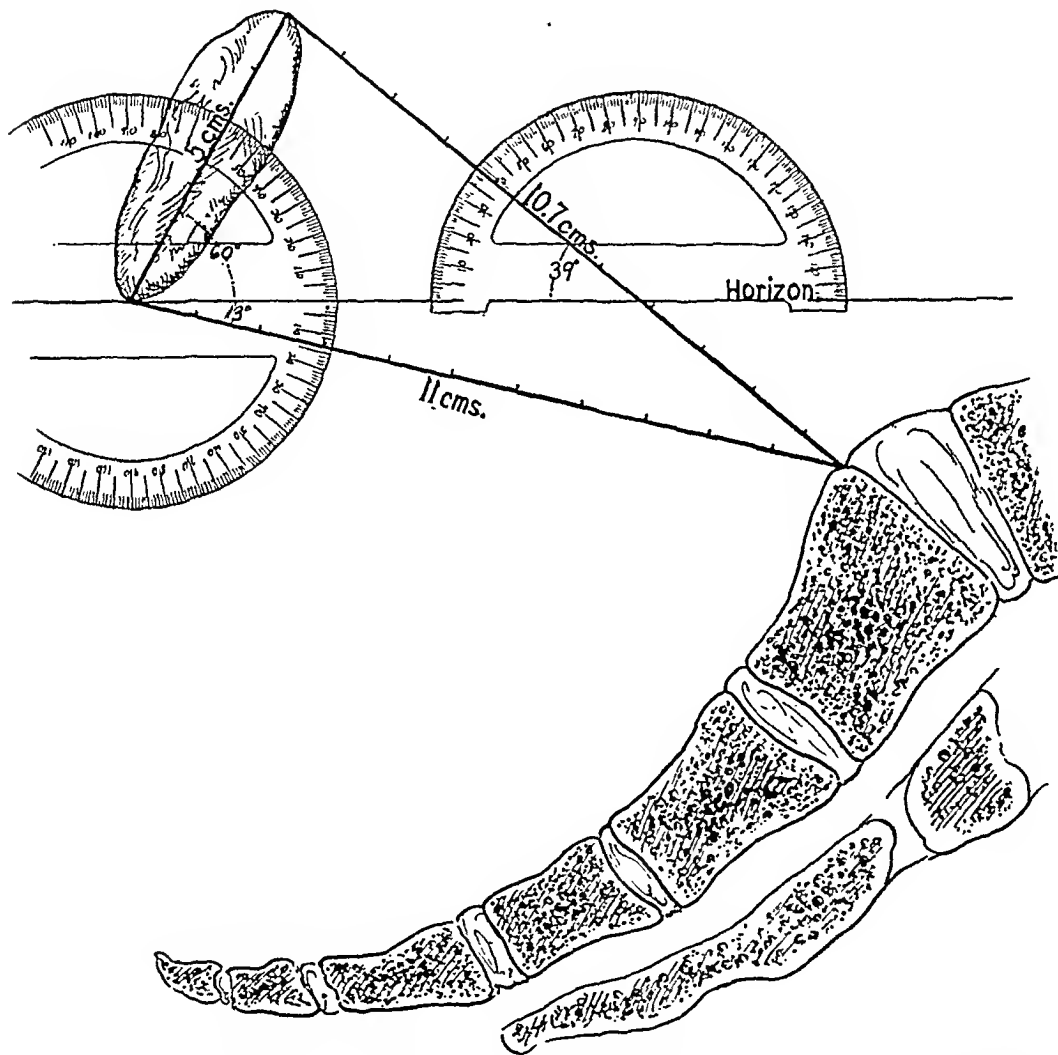


Fig. 2.—Construction of a pelvigram. After drawing a horizontal line, a protractor was used to lay off lines denoting the height and inclination of the symphysis and the length and inclination of the diagonal conjugate. These determinations were originally obtained as in Fig. 1. Symphysis and sacrum are sketched in.

A protractor is placed at the intersection of the true conjugate with the horizon and the inclination of inlet noted.

Incidentally, any roentgenographic measurement of the true conjugate should be identical with the length of this diameter as determined by the inclinometer or a pelvigram.

A tube properly placed over the inlet in this position does not subject the patient to hazard, and favors production of a clear image (Fig. 5).

My previous technic did not permit the use of a Bucky diaphragm because of its weight and bulk. The clearness that this device imparts

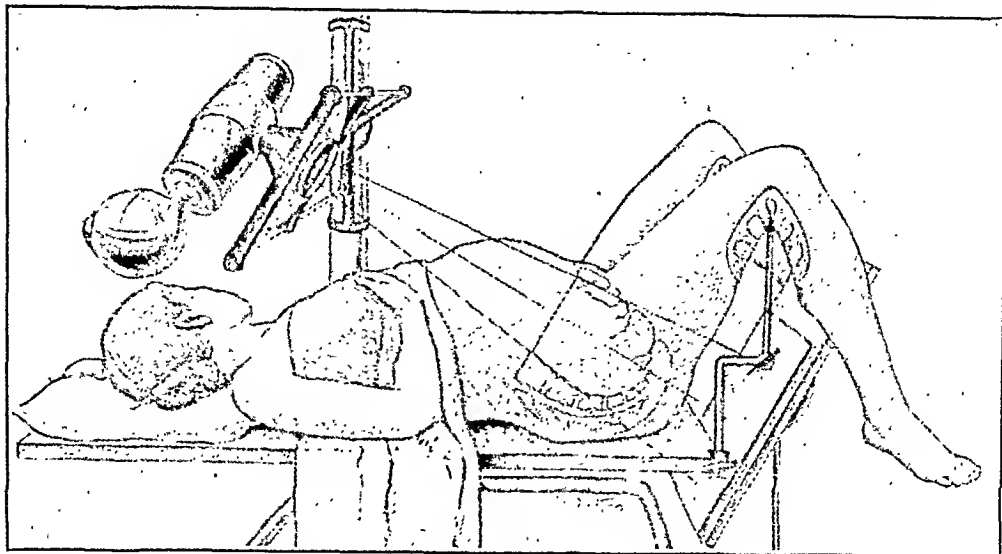


Fig. 3.—Procedure formerly followed. Flexion of thighs makes inlet approach the perpendicular to the table. For center ray to be perpendicular to the middle of the inlet, the tube must be close to the patient's face, and the rays must penetrate the length of the uterus, diminishing clearness of view. Before removing patient from the table the target to film and target to symphysis (inlet) distances are noted.

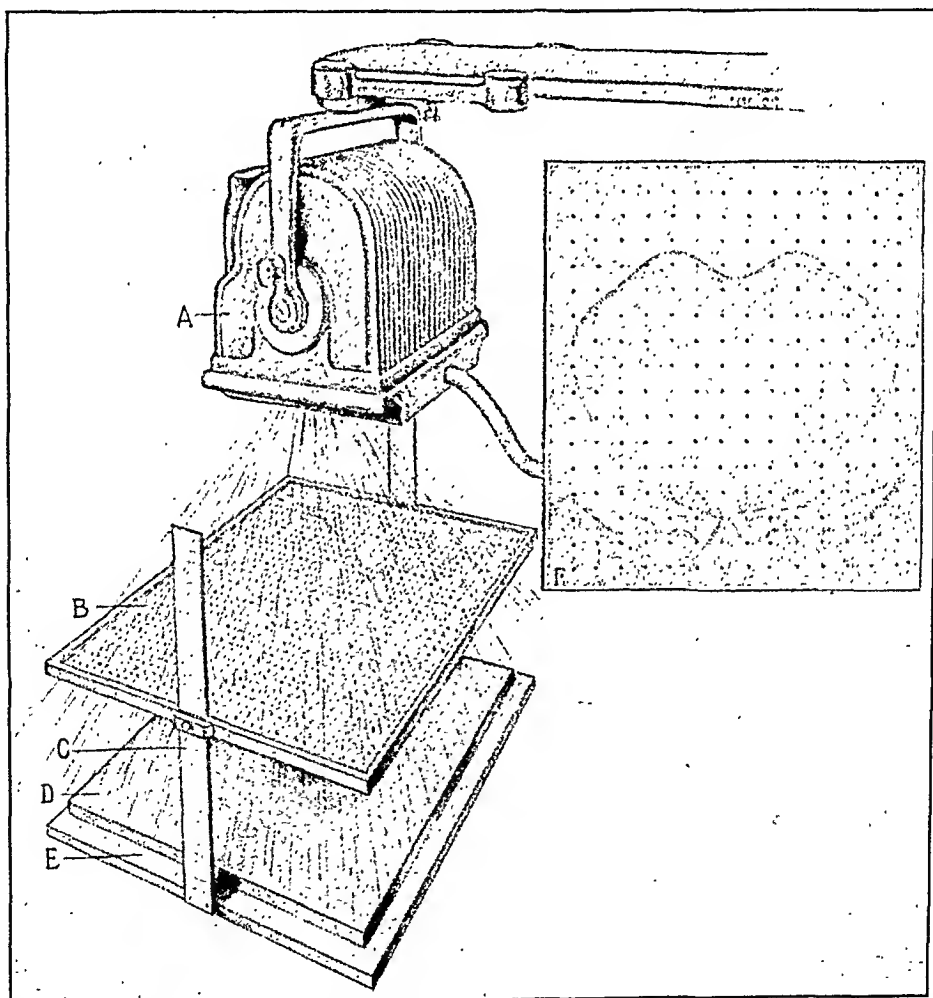


Fig. 4.—Perforated lead plate is supported by graduate holder at the station formerly occupied by the inlet in relation to the tube and film. Target is directed so center ray will be perpendicular to the middle of lead plate. Target to lead plate equals target to the inlet distance, and lead plate to film equals inlet to film distance. A, tube; B, perforated lead plate; C, calibrated rod; D, cassette containing film; E, baseboard. Insert shows doubly exposed film after being developed. The dots, signifying distances of 1 cm., are displaced in proportion to the uniform enlargement of the inlet.

to a picture is now obtained in a very convenient manner, by fastening to the anterior surface of the easette containing the film, a device recently perfected and known as a Lysholm grid. This grid is very light, measures only about one-fourth inch in thickness and may be held in place by adhesive strips. To my knowledge it is the first time that the use of this valuable piece of apparatus is advocated in roentgenographie pelvimetry.

LATERAL ROENTGENOGRAPHY

Lateral pelvic roentgenography,² in spite of its simplicity, possesses many distinct advantages. It enables observation of pelvic inclination, changes incident to rachitis, pelvic architecture, progress of descent

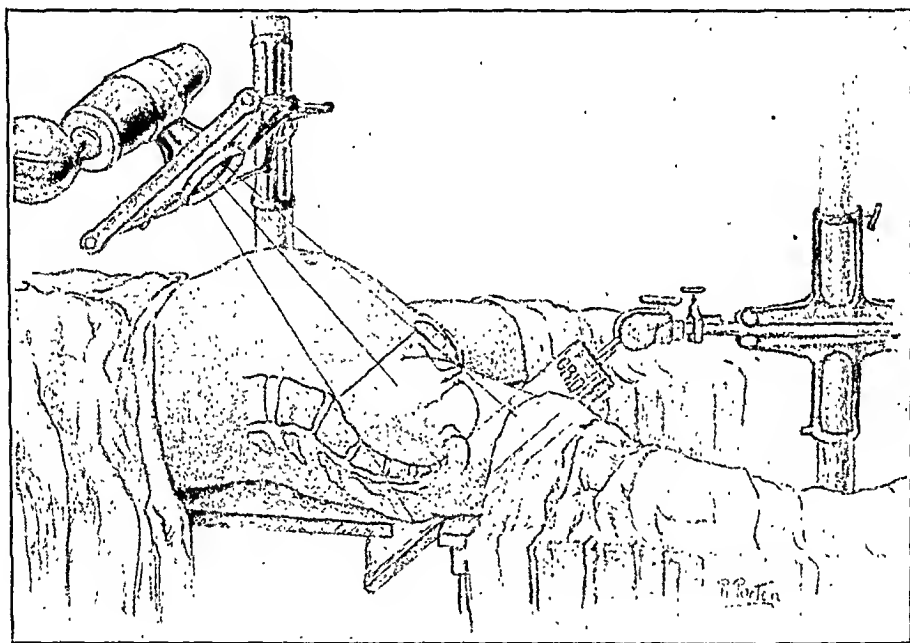


Fig. 5.—Position now used in A-P technic. Buttocks on edge of table, extended thighs are separated and supported on two specially constructed tables. Inlet in this position is more nearly parallel with table. When tube is centered, it is not as close to patient's face as in Fig. 3, and rays do not penetrate entire length of uterus. Lysholm wafer grid is fastened to cassette with adhesive strips.

during labor and mensuration of the conjugata vera as well as the fetal skull. One must be skilled in the use of the inclinometer or the technic of vaginal examination. Thus the patient is not inconvenienced to that extent and expense is diminished.

Heretofore the subject was placed on her side with legs extended.² The Bucky diaphragm and cassette which are incorporated in the table were shifted into proper position. The tube was placed so that the center ray was directed midway between the upper border of the symphysis and the bottom of the spine of the last lumbar vertebra. Exposure was made, but before removing patient from table, the target to film and target to inlet distances were noted. This film is developed and not

subjected to a second exposure using the interposed perforated lead plate previously referred to, for if it were, the dots produced by the perforations would not extend in a straight line from the upper border of the symphysis to the sacral promontory and an accurate reading would be impossible.² Therefore a second film was placed at the target to film distance and the lead plate interposed at the target to inlet distance. A

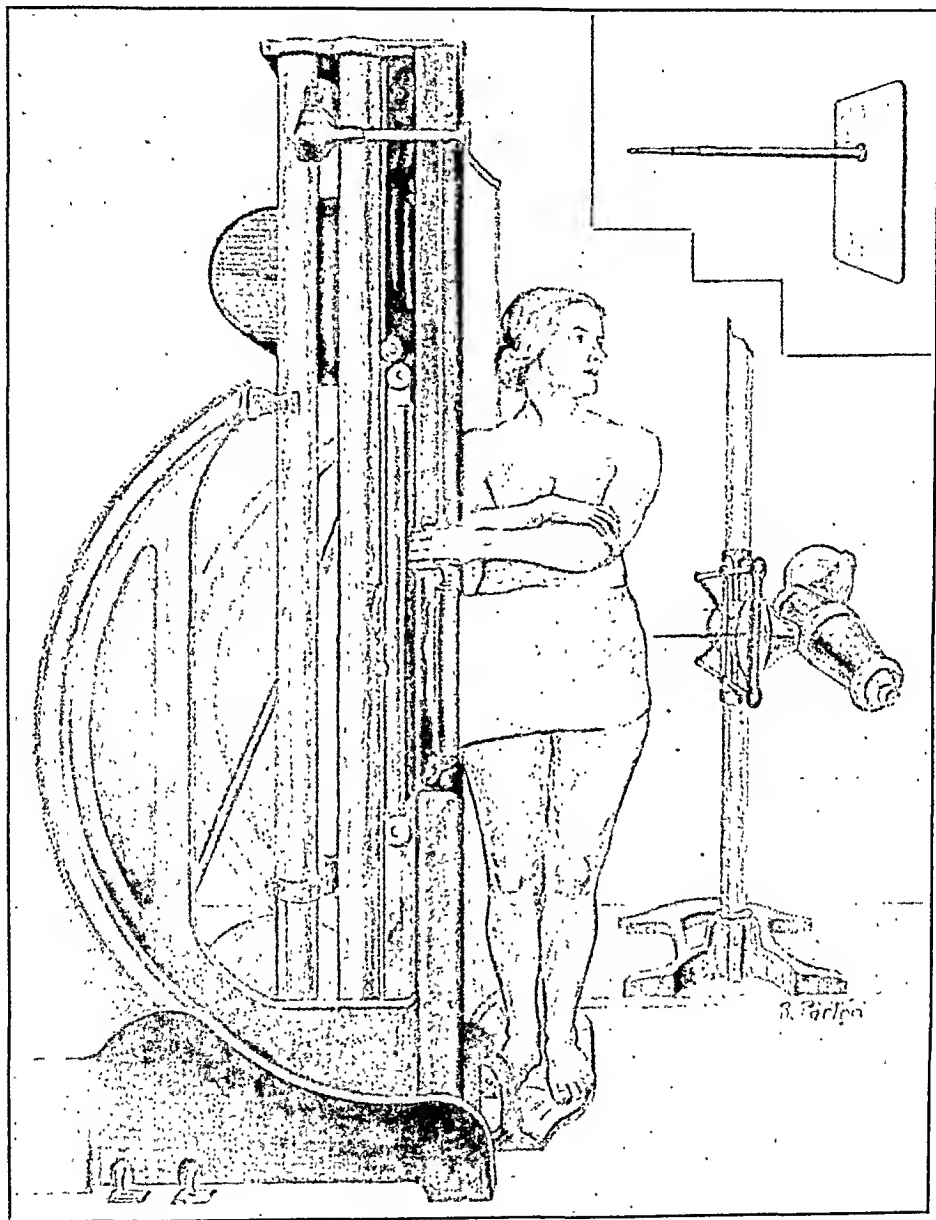


Fig. 6.—New technic for lateral pictures. Telescopic indicator shown in insert gives direction of center ray. Bucky diaphragm is used. In this posture, symmetrical points in the pelvis are more likely to be superimposed.

flash exposure transferred the dots to the film, where the distances between them is enlarged in proportion to the image of the inlet. After this is developed, it is superimposed upon the first film, so that a straight line of dots will occupy the true conjugate diameter, enabling one to read its length accurately.

The expense of this technic has been further reduced by making a flash exposure on a strip of film instead of a whole one; then this dotted seale is superimposed on the first film containing the image of the pelvis.

Improvement was effected in the following manner: The picture is taken in standing posture with the patient's hip closely applied and secured with a canvas belt, to the modern x-ray table, which readily assumes a vertical position (Fig. 6). The Bucky diaphragm and cassette may be raised or lowered to a position where the film will receive the desired image. The x-ray tube is placed so that its center ray will strike $\frac{3}{4}$ inch posterior to the anterior inferior iliac spine. This point not only lies in the plane of the true conjugate diameter, but usually denotes its middle, thus further assuring accuracy. To facilitate placing the tube, I have devised the apparatus shown in the insert of Fig. 6. It consists of a telescopic indicator fastened to a metal base in such a position that when slipped in front of the tube where it is readily ac-

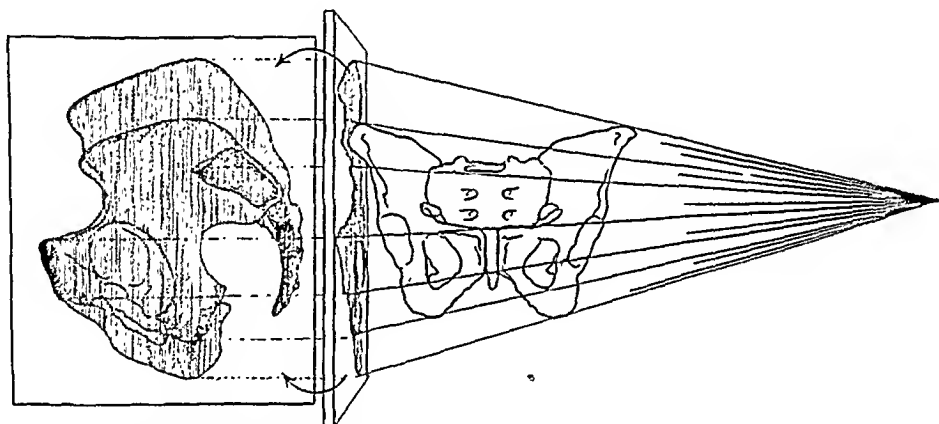


Fig. 7.—In the interpretation of lateral roentgenograms, one should realize that the half of the pelvis nearer the target casts the greater shadow.

commodated, as shown in Fig. 6, the adjustable indicator will denote the direction of the center ray as it leaves the tube. Before making exposure, this metal apparatus must be removed. The same device of course proves useful also in the anteroposterior technic, where I use it routinely.

When a picture is taken in the standing posture, symmetrical points in the pelvis are more likely to be superimposed. For when the woman lies on her side, it is not only difficult to say when she is directly on her side, but there is a tendency to rotate either forward or backward. Also, due to the contour of the normal female, the pelvis is more or less rotated through an anteroposterior axis when she lies on her side. On the film are seen the images of both halves of the pelvis. The structures on the side toward the tube will cast a larger shadow than those in contact with the table, as shown in Fig. 7. This is a factor of importance in roentgenographic interpretation of the female pelvis, which has not been emphasized in the literature.

As usual, the target to film distance, and target to inlet or symphysis (the point just above the genital crease) are noted, and the dotted strip of film prepared for purposes of mensuration.

CONCLUSIONS

The measurement of the true conjugate diameter, as determined by x-ray, should be identical in both the anteroposterior and lateral views. Readings obtained with both techniques proposed check with the calculations of the inclinometer within two millimeters.

Some authors claim accurate methods of roentgenographic pelvimetry, but have no check on their measurements, for they have no basis of comparison. One often wonders in what respects such claims are warranted.

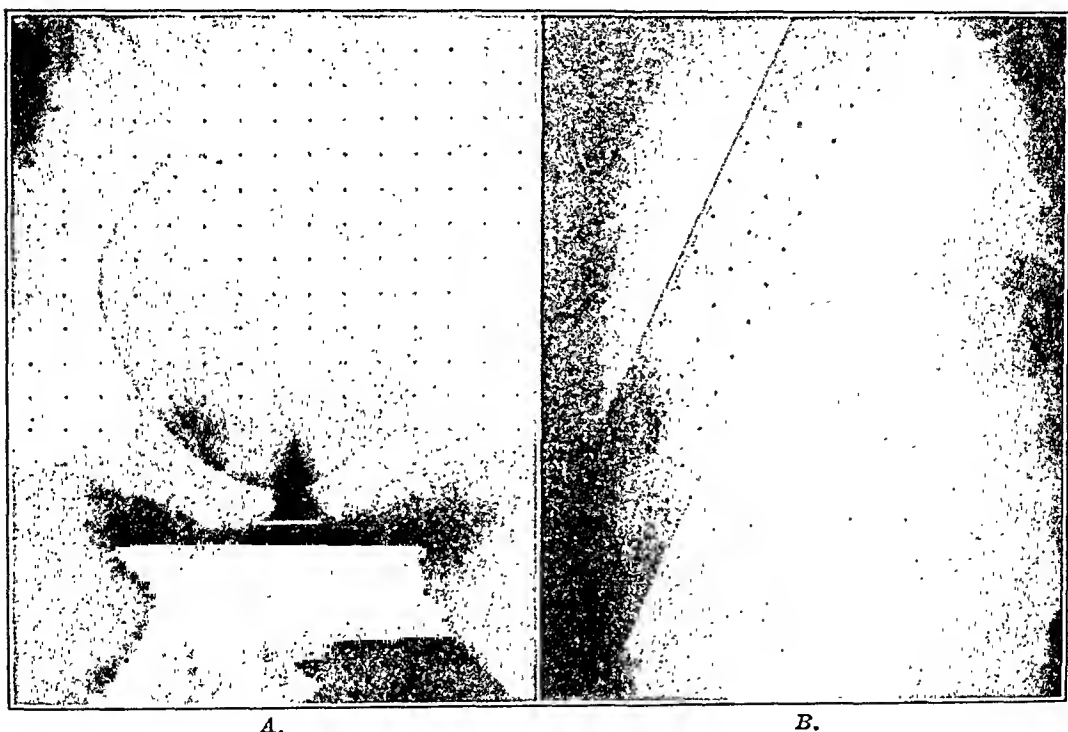


Fig. 8.—*A*, Anteroposterior view. *B*, Lateral view. By the author's technique of roentgenographic pelvimetry, measurements of the true conjugate check with calculations of inclinometer and pelvigram. Fig. 2 is a pelvigram of this patient. The pelvigram and figures here shown are evidence of an accurate study of the inlet in a borderline pelvis. T. C. measures 10.7 cm.

An acknowledged error of 1 cm. or more, in the case of a borderline pelvis, is likely to increase complications rather than spare them, because of interference with judgment.

Since the head is not a perfect sphere, the amount of error involved in mensuration of the fetal skull in the lateral view, although slight, is dependent upon rotation through its vertical axis.

Difficulty or lack of engagement due to either disproportion or faulty inclination is readily detected in the lateral view.

Pelvic roentgenography has a definite place in obstetrics, and the obstetrician should be able to interpret films as well as be familiar with

a standard technic. The simple rules of physics and mechanics should be considered in order to avoid source of error. Training may be acquired by placing small lead markers on symmetrical points of the bony pelvis, and obtaining pictures in various positions. The observations may be enlightening.

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WASHINGTON MEDICAL BUILDING

A REPORT OF THREE CASES OF PRIMARY CANCER OF THE FALLOPIAN TUBES

WITH A SUMMARY OF THE CASES OMITTED FROM NÜRNBERGER'S REPORT (1931) AND THOSE RECORDED TO 1935

M. R. ROBINSON, M.D., F.A.C.S., NEW YORK, N. Y.

PRIMARY carcinoma of the fallopian tube was recorded for the first time by Raynaud in 1847, and the first pathologic description rendered by Rokitansky in 1861. Nürnbergger ascribes priority to Orthmann who published an article on this subject in 1886.

Almost ninety years have passed since this disease entity became known, and a fairly extensive literature on primary cancer of oviducts has accumulated during this period, yet the margin of diagnostic errors, preoperatively, is as large today as it was decades ago.

In search for a reason for the persistence of diagnostic inaccuracy of this disease, it becomes evident that its rarity is the main cause. And its few pathognomonic signs and symptoms that may lead to a more accurate diagnosis are easily forgotten.

With the hope of improving the diagnosis of primary cancer of the fallopian tubes preoperatively, through a restatement and reiteration of already known but often forgotten truths, this report was undertaken.

REPORT OF CASES

CASE 1.—(Pathol. No. 8116 Beth Israel Hospital.) D. Z., aged fifty-six, consulted me on July 10, 1917, because of a vaginal protrusion. Menses began at thirteen, normal. She has given birth to one child at the age of thirty-six. Menopause began eight years ago.

Physical Examination: General condition good. Vaginal inspection showed a third degree uterine prolapse. Since the pathology was so evident, and in the absence of other symptoms, no bimanual examination was made, an inexcusable clinical error.

Operation: A vaginal panhysterectomy with a bilateral salpingo-oophorectomy, and vaginal plastic. The patient made an uneventful recovery.

Gross and Microscopic Findings: A myomatous uterus one and one-half times the normal size; an intraligamentous cyst on the right side, the size of a grapefruit, and a moderate thickening and elongation of both fallopian tubes. Histologic examination revealed a bilateral primary carcinoma of the oviducts.

Comment: In 1919 I¹ reported this case together with two other rare gynecologic conditions, and Nürnbergger² included it in his statistics. The only reason for referring to this case now is to facilitate a better grouping.

CASE 2.—(Pathol. No. 2312 Beth Moses Hospital.) F. S., aged fifty-two, consulted me on July 12, 1924, because of a profuse yellow watery, at times, bloody vaginal discharge of eight months' standing. Menses began at thirteen, regular. Married at the age of eighteen, has given birth to five normal children. The menopause set in three years ago.

Physical Examination: A tall well-developed corpulent female. Heart, lungs, urine, and blood negative. Vaginal outlet slightly relaxed, no discharge noted.



Fig. 1.—(Pathol. No. 2312, B. M. H.) Primary papillary carcinoma of the fallopian tube. The carcinomatous metaplasia is limited to the mucosa; tube wall (T. W.) not invaded as yet. The lining epithellum is multilayered, irregularly columnar, without cilia. Mitosis and degeneration in many areas. Only toward the base of the villi a single row of low columnar or cuboidal epithelium may be seen (S.R.E.).

Uterus moderately enlarged, globular in outline, freely movable and normal in consistency and size. Adnexa could not be palpated on account of the thickness of the abdominal wall. A few tender nodules were felt in the culdesac of Douglas, and one in front of the uterus in vesicouterine space. A tentative diagnosis of pelvic malignancy was made and an exploratory laparotomy advised.

Operation and Operative Findings: On June 20, 1924, I performed an exploratory laparotomy and found a normal uterus, with bilateral elongation and thickening of the fallopian tubes; the right one measured 20 cm. and the left 15 cm. in length and 5 cm. in width at the widest diameter. Right ovary moderately enlarged, cystic, and adherent to the posterior surface of the broad ligament; left ovary normal. In the culdesac of Douglas there were a few partly solid and partly cystic metastatic nodules which bled readily to touch and were fixed firmly in position. There was

another metastatic nodule, the size of a walnut in the free border of the omentum. A supracervical hysterectomy with a bilateral salpingo-oophorectomy was performed, and a resection of the tumor bearing part of the omentum.

Pathologic Findings: Sections from the fallopian tubes showed a papillary carcinoma (Fig. 1), limited to the mucosa, and growing toward the tube lumen. The epithelium covering the villi was of an irregular columnar type, multilayered, the protoplasm vacuolated, the nuclei irregular, hyperchromatic and granular. At the base of some villi a single row of low cuboidal normal-looking epithelial cells were seen. The ciliated layer was absent throughout. The connective tissue matrix of the villi showed a mild round-cell infiltration. The ovaries were normal and corresponded histologically to the age of the patient. On the germinal surface of each ovary, numerous implantation metastases were seen (Fig. 2), identical in structure with the papillary carcinoma within the tubal lumina. The endometrium was not affected by the carcinomatous spread, and showed the usual cystic dilatation and atrophy of the glands, characteristic of this period of life.

Postoperative Course and Treatment: On Aug. 19, 1924, 50 mg. of radium element were placed in the posterior vaginal fornix and allowed to remain forty-eight hours.



Fig. 2.—(Pathol. No. 2312, B. M. H.) Implanted metastatic carcinoma (I.M.C.) on ovarian surface (O.S.) from a primary carcinoma of fallopian tube. The ovarian stroma (O. Str.) is not invaded.

On Aug. 21, 1924, deep x-ray irradiation of the lower abdomen and pelvis was begun, and 110 per cent skin erythema dose was administered. For three weeks following radium and the x-ray treatment, the patient suffered from a proctitis.

Sept. 24, 1924, a pelvic examination disclosed that the nodular mass in the cul-de-sac of Douglas was no longer palpable.

Feb. 2, 1926, patient returned, stating that she had felt well up to a few weeks ago; but since then had had pain in the left side of the abdomen. Examination showed a movable tumor mass in the left upper quadrant of the abdomen. The pelvis was free from any palpable tumors. Another series of deep x-ray treatments was administered directly over the metastatic tumor. At proper intervals these treatments were repeated until June 18, 1926. During the succeeding three months repeated examinations showed unmistakable evidence of regression of the abdominal tumor; but notwithstanding this local improvement her general condition grew gradually worse, and in the early part of 1927 she died from cachexia.

Comment: A case of primary bilateral papillary carcinoma of the fallopian tubes, developing three years after the onset of the menopause, without any history of

preceding pelvic inflammation. The chief symptom complex was a profuse, watery, yellow, at times bloody vaginal discharge of eight months' standing. Although at the time of operation definite metastases were present in the culdesac and omentum, a hysterectomy with a bilateral salpingo-oophorectomy was carried out, and with the aid of postoperative irradiation this patient's life was prolonged for two and a half years during which she was comfortable most of the time.

CASE 3.—(Pathol. No. 23999 Beth Israel Hospital.) A. C., aged thirty-eight, consulted me on March 18, 1933, because of irregular uterine bleeding for the past three months. Menses began at fifteen, always regular up to three months ago. Married at the age of twenty, has given birth to three full-term normal children; the last one six and one-half years ago. Aborted once, nine years ago.

Physical Examination: General condition good. Abdomen negative. Vaginal introitus slightly relaxed. Uterus normal in position, size, contour and consistency. To the right and anterior to the uterus was an elongated sausage-like tumor; freely

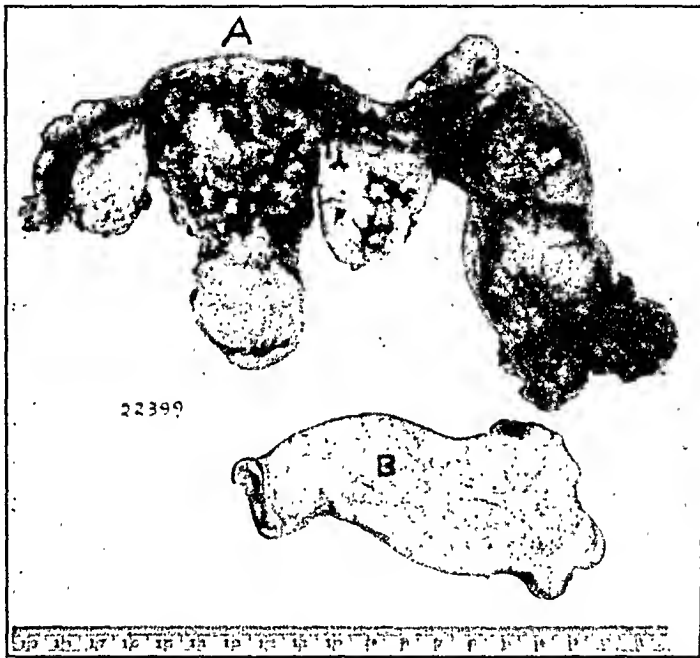


Fig. 3.—(Pathol. No. 22399, B. I. H.) Photograph of specimen of primary carcinoma of right fallopian tube (A), posterior view. At (B) the cut surface of a longitudinal section of the right tube outer half.

movable; alternately hard and soft in consistency; the outer part was about three fingerbreadths in width; and somewhat tender. The corresponding ovary was felt distinctly and independently of the tumor. The left uterine adnexa were normal to palpation. The preoperative diagnosis was hematosalpinx secondary to a torsion of the tube.

Operative Findings and Operation: On March 21, 1933, a laparotomy disclosed a slightly enlarged uterus (Fig. 3). Normal sized ovaries studded with many tiny excrescences. Similar growths were seen and felt in the vesicouterine fold. The left tube appeared to be normal. The right tube was transformed into a club-shaped mass. The isthmic portion appeared normal for a distance of 5 cm.; then an "S" shaped swelling set in; the inner half of which had a thin wall and seemed to contain fluid, the outer half was more solid in consistency. The thickness increased gradually toward the abdominal end, where it had a diameter of 5 cm. The surface showed many dilated blood vessels. The fimbrial end was occupied by thick verrucous, confluent masses. No abdominal ostium was seen. The operation consisted of a

curettage and a posterior colpoperineorrhaphy (not having suspected a malignant condition); and an abdominal panhysterectomy with a bilateral salpingo-oophorectomy.

Pathologic Report: Sections taken from the thickened part of the right tube showed a primary plexiform or alveolar carcinoma (Fig. 4) with an invasion of the tubal wall, and implantation metastases on the ovarian surfaces. The uterine mucosa was not involved.

Postoperative and Clinical Course: The operative recovery was uneventful. On the third week after the operation, deep x-ray treatment was begun. She received two skin erythema doses over the pelvic area through three portals of entry; one central and two lateral. Repeated bimonthly examinations since then have failed to reveal thus far any evidences of recurrence. The patient has gained in weight, feels well except for vasomotor disturbances due to the artificially induced menopause. Last examination, Nov. 2, 1935.

Comment: The carcinoma involved only one tube, and the visible metastases have spread chiefly by contiguity. The type of carcinoma was plexiform or alveolar; it invaded the tube wall but not beyond the peritoneal surface. The uterine bleeding

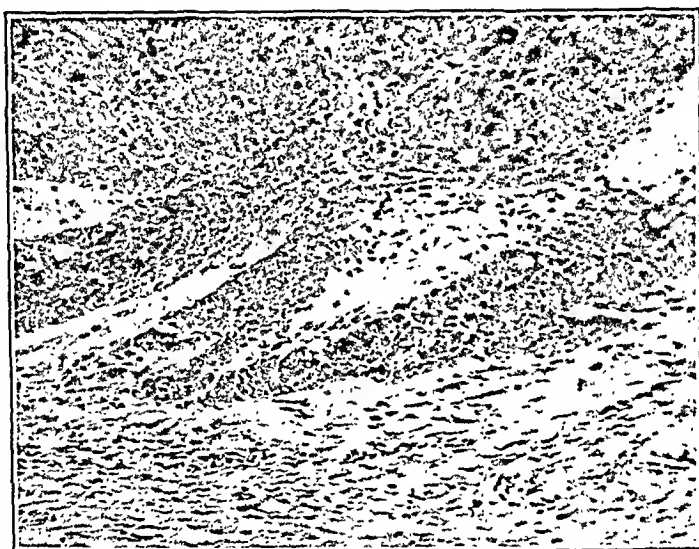


Fig. 4.—(Pathol. No. 22399, B. I. H.) Primary carcinoma of right fallopian tube; alveolar type. Note invasion of tube wall. Serosal surface normal.

in this case was not functional as shown by the curettage, and must have been due to the same factors that cause uterine bleeding in inflammations of the uterine adnexa; or perhaps to a discharge of the tubal contents into the uterine cavity from time to time, which is frequent in tubal carcinoma.

In 1932 Nürnberger² published his collection of 301 cases, covering the period from 1886 to 1931. I have collected forty-eight cases dating from 1931 to 1935, including those omitted by Nürnberger and my additional two cases embraced in the present report. All in all there are now 349 cases of primary tubal carcinoma recorded in the literature up to 1935.

1. *Frequency.*—From the statistics published by Zangemeister,³ Barrows,⁴ Wharton and Krock,⁵ and Gupta⁶ we learn that the range of frequency of primary tubal cancer in gynecologic affections may vary from 0.03 to 0.31 per cent.

2. *Age.*—Like any other form of carcinoma, primary tubal cancer may affect the young as well as the old. In this series of 48 cases, 2 occurred at the age of eighteen

and 2 at the age of seventy. The preponderance of cases occurred between the fourth and the fifth, and between the fifth and the sixth decades, respectively.

3. *Etiology.*—Sanger and Barth⁷ proffered the theory of a preceding salpingitis as a predisposing cause to primary tubal cancer. Many others accepted this viewpoint. Subsequent studies by Pehan,⁸ Vest,⁹ Kehrer,¹⁰ Stoltz,¹¹ Wechsler,¹² Liang,¹³ and others did not substantiate this claim. Frankl¹⁴ states: "If inflammation would be the precursor of primary cancer of the fallopian tube, then the incidence of malignancy ought to be much higher, for salpingitis is overwhelmingly frequent." We must admit then that the theory of salpingitis as a predisposing factor to malignancy is as tenuous as all the other theories propounded concerning the cause of malignant growths in general.

4. *Pathology.*—The diagnosis of primary cancer of the fallopian tube is based on proving that the genetic source is the endosalpingium. This can be easily established during the earlier phases of the disease, when anatomical landmarks are still recognizable. The finding of a cancer particle in the tube lumen, as seen in Fig. 5, does



Fig. 5.—(Pathol. No. 1282, B. I. H.) Secondary carcinoma of fallopian tube. Carcinomatous nests within the stroma and tube lumen, epithelium not involved.

not speak for its primacy in the tube, even after it has engrafted itself upon the lining epithelium. According to Sampson¹⁵ and Wallbruch,¹⁶ these cancer masses are broken off particles from a malignant endometrium, forced into the tube lumen. Another pathologic fact purporting the diagnosis of primary tubal cancer is the late involvement of the tube wall, while in cases of secondary carcinoma, the tubal wall shows cancer deposits with a normal overlying mucosa.

Friedenheim¹⁷ and others among the earlier pathologists described three types of tubal carcinoma, the papillary, the adenomatous, and the alveolar. I am in full accord with the views of Liang¹³ that such classifications are superfluous and confusing, for these different morphologic appearances do not denote distinct types of cancer but different phases in the evolution of the same malignant process. The papillary is the earliest, the alveolar the latest, and the adenomatous the intervening phase. I have found frequently two phases in one and the same tube, and normal looking tubal epithelium, except for loss of cilia, next to definitely cancerous. All these facts speak for the evolutionary character of malignant processes.

Primary carcinoma of the fallopian tubes is frequently bilateral. This pathologic fact is of utmost clinical importance. The apparently normal looking opposite tube should not deter us from a radical procedure. This rule is also applicable to ovarian malignancy. The outer two-thirds of the tube are the sites of greatest predilection. When the fimbriated end becomes closed, which is a late phenomenon in contrast to gonorrheal salpingitis, which occurs early, the tube may reach enormous dimensions, due to distention with secretions and necrotic tissue elements.

From the fallopian tube the cancer may spread to other tissues and organs by continuity, contiguity, or lymphatic extensions. This subdivision of metastatic routes into three forms is arbitrary and purely didactic. It can be stated safely that the lymphatic route is the only one, and this is based on the clinical and pathologic observations made by Hudson,¹⁸ Cullen,¹⁹ Liang,¹³ Vest,⁹ Callahan,²⁰ and others that metastases from primary tubal cancer may be found in remote locations long before the tubal wall becomes involved.

The fact that particles of cancer tissue may be transported from the uterine cavity to the tube lumen speaks for the even greater possibility of cancer particles to be carried from the tube lumen into the uterine interior. When this occurs and the cancer becomes engrafted upon the endometrium, a diagnostic curettage in such an instance may lead to an erroneous interpretation as to the origin of the cancer. This is of academic interest only, for clinically the therapeutic procedure would be the same.

5. *Symptoms and Signs.*—The most common and chief complaints are pain in the lower abdomen and yellow, watery or bloody vaginal discharges. On careful inquiry it is possible to elicit at times that the character of the pains is intermittent, that the vaginal discharge is of an amber color, and that the pains disappear after a sudden gush of watery, yellow or bloody fluid from the vagina. This symptom complex was first noted by Latzko²¹ and later described in detail by Stanca.²² These authors termed this symptom complex "hydrops tubae profluens," and explained its biomechanism as follows: "The colicky intermittent pains are due to exaggerated tubal peristalsis evoked by the effort to expell the fluid and semisolid contents the result of enoplastic growth and necrosis. As soon as these tissue elements are expelled into the uterus and from there into the vagina the pains cease suddenly."

Physical examination of the pelvis helps but little in establishing a preoperative diagnosis of primary tubal cancer, since the findings simulate closely those of salpingitis due to other causes.

6. *Treatment.*—Early radical operation followed by deep x-ray therapy is the most conservative form, for it offers the best prognosis.

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THE PROGESTERONE TREATMENT FOR DYSMENORRHEA

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THE uterus of the experimental animal has been shown to be in a state of motility, and definite contractions can be recorded when the animal is in a state of estrus. Under the influence of the animal's own corpus luteum the uterus becomes quiescent, no contractions can be elicited, and it is refractory to pituitrin.¹⁻⁴ The uterus of the pseudo-pregnant rabbit, a state comparable to the last half of the menstrual cycle in the human being, reacts according to Knaus¹ in the same way. Reynolds⁵ has developed a method of studying uterine motility in the unanesthetized rabbit. His observations^{6, 7} are in accord with those of Knaus. Recently,⁸ it has been shown that estrin and progesterone containing extracts are the two hormones responsible for the physiologic findings established by Knaus and Reynolds. Knaus⁹ and Wittlebeck¹⁰ have demonstrated by kymographic record that the human uterus in vivo is in a state of motility and contractility up to the sixteenth day of the menstrual cycle, and that from the sixteenth day to the day before the onset of menstruation it is flaccid, sluggish, and does not react to pituitrin. On the day before the onset of menstruation the uterus reverts to its preovulatory behavior, a fact which may help to explain the cause of dysmenorrhea in some instances. It has been noted by one of us (C. A. E.) in endometrial studies on five human castrated females¹¹ that one of the patients who had had dysmenorrhea all her life suffered with the same pains when she was given sufficient estrin to establish bleeding. When the same amount of estrin was given followed by progesterone she had no pains. This procedure was repeated several times with the same results. It should be noted that only one of the five castrated human females had dysmenorrhea when given the same amounts of estrin to induce bleeding. Therefore estrin alone cannot be the sole cause of this symptom complex. No doubt that contractions occurred in the uteri of all patients under the influence of estrin. It is highly probable that the one patient had a lowered sympathetic threshold for pain caused by the contracting uterus or that the congestion produced by the hormone prior to the bleeding was sufficient to account for the pain. The progesterone may have sufficiently relaxed the uterus so that the contractions were not perceptible or that circulation was re-established, thus relieving the pain.

With progesterone available (prepared by one of us [C. A. E.] by established methods¹² and supplied by the Schering Corporation) the

following seventeen selected patients were treated with small doses of the hormone. The amounts used were at first chosen empirically and given either in divided or single doses three to six days before the menstrual flow or before the onset of pain. It was given at this time because of Knaus' observation⁹ that the uterus reacts to pituitrin the day before the onset of bleeding and because the hormone is in oil and therefore slowly absorbed. Some forty patients were treated from which seventeen were selected for further study. Those not included in this series were either relieved by progesterone and subsequent doses of sterilized oil or other ineffective materials, or they had obvious psychic disturbances which made any evaluation of the effect of the hormone impossible. In the cases presented if the patient obtained relief with the hormone, she was subjected to one of two types of control. Either she was given injections of sterilized oil or no medication at all. If pain followed, progesterone therapy was reinstituted. If only partial relief was obtained larger doses were given. It should be pointed out that if the hormone is given too early or too late it is without effect, hence an accurate menstrual calendar and prompt injections are necessary for success.

The following observations were made: first, results of progesterone therapy on the relief of pain, and second, the effect of the hormone on the interval, duration and character of the menstrual period. These observations are in the case histories given below. In none of the patients, except as noted, was there any pathologic condition, anatomical malformation, or obvious psychic disturbance which could account for the symptom complex.

PATIENTS TOTALLY RELIEVED

CASE 49651 was a sixteen-year-old single female who had suffered with dysmenorrhea since the onset of catamenia. Menstrual cycle $14 \times 24-28 \times 5$. Pelvic organs normal. She was given $\frac{3}{25}$ Rb. U. progesterone on Dec. 17, 1934, and the menstrual period started Dec. 22, 1934 with complete relief. The same dose was given on Jan. 16, 1935, and the period started Jan. 19, 1935, with complete relief. As a control she was given sterilized oil before the next period, and menstrual flow started Feb. 18, 1935, five days after injection, with a return of dysmenorrhea. She was given the same dose of progesterone March 16, and menstruation started March 21 without pain. Medication was repeated in April with relief. A two-month control period was started during which no medication was given. The patient left town for the following three months making a control period of five months. During this time she menstruated regularly and had dysmenorrhea with each period. She was again given $\frac{3}{25}$ Rb. U. of progesterone on October 16, and menstruation started October 19 with complete relief of pain. The following months she was given no medication, and the period started November 16 with pain. The next few periods were without pain because of the administration of the hormone. When the dosage was reduced to $\frac{1}{25}$ Rb. U. on one occasion the patient experienced slight pain.

CASE 91295 was a twenty-eight-year-old married female who had always had dysmenorrhea. Except for being mildly hypothyroid she was physically normal, and pelvic examination was normal. The same procedure was followed on this patient, with control periods during which she received no medication and experienced pain

with menstruation. On two occasions the progesterone was given the day before the onset of the period and in both instances she suffered pain. This patient has been followed eighteen months under controlled conditions with relief of pain.

CASE 15249 was a twenty-four-year-old married female who began menstruating at thirteen. Her menstrual periods were every twenty-eight days, lasting five days, always accompanied by dysmenorrhea. The pelvic examination was normal. She was given $\frac{1}{25}$ Rb. U. of progesterone Sept. 1, 1935, and menstruation started September 4 with complete relief of pain. The following month she was given an injection of sterilized oil, and the period started October 2 with dysmenorrhea as severe as originally. For the next two months she was given $\frac{3}{25}$ Rb. U. progesterone with complete relief, and the menstrual periods were on time.

CASE 71913 was a sixteen-year-old single female who had always had slight dysmenorrhea. Following a gum shot injury to the frontal lobe, for some reason or other the dysmenorrhea became worse. The cycle was $15 \times 28 \times 5-6$; pelvic examination was normal. The first injection was given too early, hence she got no relief. A dose of $\frac{3}{25}$ Rb. U. was given Aug. 27, 1935, and the period started September 5 without relief. The next injection of the hormone was given September 29, and the period started October 2 with complete relief. The next month complete relief was obtained, and the following two months no medication was given. In each instance there was a return of the dysmenorrhea, and progesterone therapy was reinstituted with complete relief, and no change in the menstrual cycle.

CASE 100206 was a thirty-two-year-old single female who had always suffered with dysmenorrhea. Her menstrual cycle was $16 \times 28-31 \times 3$. The first injection of $\frac{3}{25}$ Rb. U. was given Mar. 14, 1935, and the period started March 23, accompanied by dysmenorrhea. Evidently the hormone was given too early for effect. An injection of $\frac{3}{25}$ Rb. U. was given April 16, and the period started two days later with complete relief. A two months control period was instituted, during which the cycles were normal, and the patient suffered with dysmenorrhea. Progesterone therapy was again established for the next three months with complete relief. During the next four months' control period the patient always had dysmenorrhea. She was then given $\frac{3}{25}$ Rb. U. of progesterone each of the next three months with complete relief. In no instance throughout the study was there any change in the menstrual cycle.

CASE 102244 was a twenty-three-year-old single female who had suffered with dysmenorrhea from the onset of the cycle at fourteen. Periods were about every thirty-five days, lasting seven days. Progesterone therapy was instituted June 15, 1935, at which time $\frac{3}{25}$ Rb. U. was given and the period started June 18 with complete relief. The procedure was repeated for the next period with relief. The third period was used as a control and the patient experienced pain. Progesterone was given for the next two menstrual cycles with complete relief. There was no delay in the period and the constitutional symptoms were much less severe.

CASE 105009 was a thirty-three-year-old married female with normal pelvic organs who always suffered with dysmenorrhea. Her menstrual cycle was $15 \times 28 \times 6$, with pain beginning about one week before. Therefore $\frac{3}{25}$ Rb. U. was given three times beginning ten days before the onset of the expected period. The first period was attended by some relief, as was the second and third. The cycle in all instances was not delayed by using three times the hormone ordinarily administered. The next period was used as a control, and the original symptoms returned. Subsequent therapy has given good results.

CASE 93088 was a nineteen-year-old single female who had mild dysmenorrhea for the first seven years since the onset of menstruation. The next year the pains were more severe and the past year unbearable. Her menstrual cycle was $11 \times 28 \times 5$,

and pelvic examination was normal. She was given $\frac{3}{25}$ Rb. U. progesterone for six months following the usual procedure, with complete relief. There was no change in the menstrual cycle. No therapy has been given for the past six months, and only mild symptoms have returned which do not require therapy.

PATIENTS RECEIVING SOME RELIEF

CASE 93695 was a twenty-two-year-old single female, with normal pelvic findings and menstrual cycle $15 \times 28 \times 6-7$. She had always had some dysmenorrhea which became worse in the past year. She was given $\frac{3}{25}$ Rb. U. of progesterone October 17, 1934, and the menstrual period started October 21 with no relief. The dose was doubled the next month with some relief, and in December $\frac{1}{2}$ Rb. U. gave some relief. For the January menstrual period no medication was given with the result that dysmenorrhea was severe. Another $\frac{1}{2}$ Rb. U. was given Feb. 1, 1935, and the period started February 6 with some relief. No medication was given in March, and the period was accompanied by severe dysmenorrhea. During each of the following two months $\frac{9}{25}$ Rb. U. was given as she claimed as much relief with this dose as the $\frac{1}{2}$ Rb. U. Pains in both instances were relieved in part. This might be a case of secondary dysmenorrhea, although nothing in the history or examination gave any indication of same.

CASE 23279 was a thirty-four-year-old female who had always had dysmenorrhea. The pelvic findings were normal, menstrual cycle $14 \times 28 \times 5$. She was given $\frac{2}{25}$ Rb. U. Oct. 3, 1935 with little relief. The next month no medication was given and she suffered considerable pain. In April the dose was increased to $\frac{4}{25}$ Rb. U. with some relief. No medication was given in May, and pain was severe. The dose was increased to $\frac{9}{25}$ Rb. U. for June with almost complete relief. No medication was given in July. The patient has not been seen since then.

PATIENTS RECEIVING NO RELIEF

CASE 1593 was a twenty-eight-year-old married female with normal pelvic organs who had always had dysmenorrhea. Her menstrual cycle was $14 \times 28 \times 5$. She was given varying doses up to $\frac{9}{25}$ Rb. U. on four occasions with no relief whatever.

CASE 94387 was a twenty-year-old married female with normal pelvic findings, menstrual cycle $13 \times 28 \times 3$. The dysmenorrhea started at the age of fourteen and has persisted to date. All types of medication were without avail. She was given varying doses of progesterone up to $\frac{1}{2}$ Rb. U. for a period of four months without relief. The pain seemed to have been worse. This patient's difficulties were severe enough to warrant a presacral sympathectomy, following which there was complete relief of pain. At operation the pelvic organs were normal in every respect.

CASE 43864 was a nineteen-year-old single female with normal pelvic findings, menstrual cycle $14 \times 35 \times 7$, who had always suffered with dysmenorrhea. She was given varying doses of progesterone up to 1 Rb. U. (some in divided doses) and in one of the five times some relief was obtained. Her pains were severe enough to warrant a presacral sympathectomy, following which complete relief was obtained. The pelvic organs at laparotomy were normal.

CASE 40101 was a twenty-seven-year-old single female, menstrual cycle $12 \times 31 \times 6$, who had always suffered with dysmenorrhea. Pelvic examination was normal. She was given varying doses of progesterone up to 1 Rb. U. over a period of six months without relief. Estrogenic preparations (progynon-B) in doses up to 50,000 international units were without effect. In no instance with either medication was there any change in the menstrual cycle.

CASE 40218 was a twenty-five-year-old married female, menstrual cycle $13 \times 31 \times 5$; pelvic examination revealed an infantile uterus. She had always had dysmenorrhea, and received no benefit from doses of progesterone up to $\frac{9}{25}$ Rb. U. over a period of three months. No doubt a factor in this case was the infantile uterus.

CASE 28290 was a fifteen-year-old female, single, menstrual cycle $12 \times 28 \times 4$, pelvic organs normal, who had always had dysmenorrhea. She was given doses of progesterone up to $\frac{9}{25}$ Rb. U. on four occasions without relief. Twice she was given progynon-B with no relief, though the estrogenic material did not make the pains worse.

CASE 85749 was a twenty-nine-year-old married female who had always had dysmenorrhea which had become worse in the past four years. Five years ago she had an abortion with questionable infection. Pelvic examination revealed normal organs and no evidence of pelvic inflammatory disease. She was given doses of progesterone up to $\frac{9}{25}$ Rb. U. on 6 occasions with only partial relief in one instance. Possibly the dysmenorrhea was secondary to the infection.

COMPLETELY RELIEVED	PARTIALLY RELIEVED	NO RELIEF
8	2	7
47.0%	11.7%	41.3%

From these observations it was noted that 47.0 per cent of the patients obtained complete relief with doses of progesterone varying from $\frac{2}{25}$ to $\frac{9}{25}$ Rb. U. Two of the patients or 11.7 per cent claimed only partial relief and did not get total relief with larger doses of the hormone. The remaining 41.3 per cent received no benefit from therapy. In the latter group there was one case of infantile uterus and two in which there was a question of old pelvic inflammatory disease, although nothing pathologic could be demonstrated on pelvic examination.

There was no delay in the onset of the menstrual cycle caused by the small doses of progesterone and apparently no change in the duration or character of the menstrual flow.

Those patients benefited by the hormone had some relief of constitutional symptoms and one of the patients had relief of constitutional symptoms and only partial relief of the pain. Two patients not relieved by progesterone or any other known remedy subsequently had pre-sacral sympathectomies with complete relief. The pelvic organs at operation were normal in all respects.

DISCUSSION

That progesterone has an experimental background for the treatment of dysmenorrhea has been established. One can infer that there are certain types of dysmenorrhea which are hormonal in nature, and it is this group in which benefit is possible with progesterone. One of the patients receiving no benefit at all had an infantile uterus which in itself may account for lack of relief. It seems strange at the moment that such small doses of the hormone can give complete relief, yet when one considers the fact that a pituitary reaction can be elicited just before the menstrual period in the human being⁹ and that small doses cause relaxation in the uterus of the rabbit,⁸ it is highly probable that an effect takes place in the human being. Relief may be explained on the basis of Schröder's theory of dysmenorrhea in that sufficient relaxation of the uterine musculature is obtained to insure adequate circulation thereby overcoming added congestion normally present at this time.

That some of the failures may be due to improper balance between the several hormones operating at this time must be kept in mind. In fact, two of our patients were made worse by the use of progesterone. Our exact knowledge concerning the interrelation of the hormones of the body is only fragmentary. Continued application of this hormone under controlled clinical conditions will eventually bring to light a better understanding of its use. That estrin alone is not the sole factor in the causation of dysmenorrhea has been demonstrated.¹¹ The rôle of the sympathetic nervous system in normal and pathologic physiology of menstruation and histologic studies of uterine musculature in this field still remain to be solved before the problem of dysmenorrhea can be finally solved.

CONCLUSIONS

Seventeen selected patients with dysmenorrhea were treated with progesterone. Forty-seven per cent obtained complete relief, 11.7 per cent claimed partial relief, and 41.3 per cent received no relief. The doses varied from $\frac{2}{25}$ to 1 Rb. U. given in single or divided doses three to six days before the onset of the menstrual flow. The possible mechanism is discussed. There was some relief of constitutional symptoms in some of the cases. This was not a constant finding. There was no delay in the onset of the menstrual flow nor any change in the character or duration of the period caused by the small doses of the hormone.

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The author together with Dr. C. C. A. Croin saw within the last two years six cases of chronic retention of urine in women, all suffering from a syndrome similar to that of prostatic enlargement. The bladder showed some trabeculation, sometimes saecules. The urethra was neither compressed nor obstructed. The trouble was located at the bladder neck, indicating a difficulty in relaxation. To this condition Leguen has applied the term "dyseetasia." The retention could not be attributed to disease of the central nervous system. In one case, however, there was a spina bifida, and another patient suffered from Parkinson's disease. All these cases were treated with Caulk's cautery punch and either cured or greatly improved.

HUGO EHRENFEST.

THE USE OF PARALDEHYDE ANALGESIA IN LABOR

INCLUDING STUDIES OF THE EFFECT UPON THE UTERINE CONTRACTION

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DURING the past few years much effort and ingenuity have been expended in the attempt to discover the perfect method for ameliorating the distress associated with childbearing. Many technics have been offered, most of which have for a base some of the barbiturates. A number of these are fairly successful when used by those experienced in the method, but all are not without certain disadvantages. However, from the progress which has been made, it appears inevitable that the ideal method will some day be described. For this reason, each new idea presented seems worthy of adequate study and clinical trial in the interests of progress along this line. Such a "new idea" is that based upon the use of paraldehyde, alone or in combination with other drugs. At the present time paraldehyde is in the stage of experimental clinical use, but the reports which are accumulating tend to establish it as one of the more successful methods.

Rosenfield and Davidoff, in 1932, presented a preliminary report on the use of paraldehyde in 50 cases of labor. Later, in February, 1935, they presented a more complete study of 300 cases. Almost simultaneously with this last report Colvin and Bartholomew reported the use of paraldehyde in 100 cases, and Kane and Roth in 175 cases. The method varied quite considerably in each series, but the results were satisfactory in most cases. Rosenfield and Davidoff combined paraldehyde with sodium pentobarbital, without which they felt that paraldehyde was ineffective. These authors administered the medication early in labor and often repeated the dose when necessary. Colvin and Bartholomew used paraldehyde with sodium amytal, but did not begin the medication until labor was well into the first stage and did not often repeat the initial dose. Kane and Roth advocated the use of paraldehyde as often as the condition of the patient may warrant. In all of these series no ill effects were noted in either the mother or the fetus, and recovery from the drug was prompt in all cases.

A study of the use of paraldehyde in labor was begun at Cleveland City Hospital in June, 1934. At the onset of its use so little was known about the drug that no routine could be followed, and the preliminary series of 50 cases included various technics and combinations of drugs. Concerning our initial efforts in the use of paraldehyde, it will suffice to say that our results were encouraging enough to lead us to continue our studies. In all, this initial series consisted of 50 cases. In most the drug was given rectally with an equal amount of olive oil, the usual dose

of paraldehyde being six drachms, repeated every three or four hours. In some cases the drug was combined with morphine, sodium amytal, or sodium pentobarbital. In 64 per cent of these cases the results were satisfactory, while in 22 per cent the results were poor. The greatest difficulty seemed to be in poor absorption of the drug from the rectum. Also, in the dosage used, labor was definitely slowed. With this experience gained, however, it was possible to proceed with a more fixed routine and a more definite objective. The results obtained in our last 100 cases offer more which may be said in favor of the use of paraldehyde.

TECHNIC

Administration.—Following the initial series of cases in which various techniques and dosages were used, a method similar to that recommended by Kane was evolved which was used consistently in our last 100 cases. The manner in which the drug was administered has seemed to be of primary importance. Preparation of the patient was begun as soon as she was admitted to the hospital in labor. This consisted of the usual procedures plus an additional cleansing of the lower bowel by means of two or more cleansing enemas, an important detail which may lead to failure if neglected. If the patient, after rectal examination, seemed to be suitable for paraldehyde the prepared dose of the drug was administered. It was found desirable to give the drug high in the rectum, followed by an ounce or two of normal saline solution. The rectal tube was withdrawn quickly, and the anus was held with a pad for twenty minutes. During the instillation, the patient was encouraged to breathe deeply, and if the pains were severe, it was occasionally necessary to administer a small amount of ether by inhalation. After twenty minutes the drug usually was well retained.

Indications.—Paraldehyde has seemed to be equally suitable for use in primiparous and multiparous women. However, in order that the drug may be most effective, it must be given at least three hours before delivery. For this reason its use was limited to multiparas with no more than 4 cm. cervical dilatation and primiparas with no more than 7 cm. dilatation. It was our purpose to begin the medication as soon as it could be ascertained definitely that labor was established, and therefore it was most often given when there was much less cervical dilatation than this. An effort always was made to begin medication when the discomfort of the patient warranted it rather than wait for any designated thinning or dilatation of the cervix. With regard to the physical condition of the patient, no contraindications to the use of the drug were recognized. As yet, however, too little is known to say that it is safe to use it in all cases, and it would seem advisable to select patients in whom there is no marked disability such as anemia, toxemia, or exhaustion.

Dosage.—In our last 100 cases the dosage of paraldehyde used by Kane was employed, and it was found to be the most satisfactory. It is based upon the total body weight of the pregnant patient and seems more rational than any haphazard large or small dose. In this method each dose consists of 1 c.c. of paraldehyde per nine pounds of body weight with an additional 3 c.c. to the total amount. To this also is added 1.5 c.c. of benzyl alcohol. There seems to be little doubt that the benzyl alcohol, because of its local action in the bowel, facilitates the retention and absorption of the medication. Aside from a small amount of normal saline solution which was used to flush the medication into the rectum, nothing further was added. The use of the various oils with the paraldehyde was abandoned because there was much slower and less complete absorption with this combination.

After the initial dose of paraldehyde further medication was based entirely upon the patient's reaction and the hypnotic effect secured. Often, within half an hour after the first dose was given the patient slept soundly and seemed to be experiencing no discomfort. This observation leads us to disagree with Rosenfield and Davidoff, who feel that paraldehyde is ineffective without supplementary medication. In most cases, however, analgesia was intensified when additional drugs were used. Whether or not supplementary medications were included, a second dose of paraldehyde was given within two to four hours after the first dose; thereafter the dose was repeated as often as necessary to secure the desired degree of hypnosis. When several doses had been absorbed, the patient usually slept soundly through the contractions, and the interval between doses could be extended to four or six hours if the labor was prolonged. The desired objective was to deepen gradually the hypnosis by repeated doses of the medication until analgesia was at a maximum and amnesia complete. The degree of hypnosis at the onset of treatment was intensified by the use of other suitable drugs. When the optimum reaction was reached, the patient could be maintained easily for many hours if necessary.

Supplemental Drugs.—In order to secure the best results from paraldehyde, it was often necessary to give additional medication, especially at the outset of treatment. The best results were obtained by the judicious use of morphine, but it was preferred not to give this to multiparas in whom sodium amytal was substituted. It was the practice to give one of these if the first dose of paraldehyde seemed to be ineffective after forty-five minutes, or if the patient was extremely uncomfortable when the medication was begun. In certain instances it was necessary to repeat the morphine, usually if delivery was delayed or restlessness became marked.

Management of Treatment.—Needless to say, a wide variation in the individual reaction to paraldehyde was noted. After a single dose of the drug, some patients could be managed for many hours without additional medication. In a few isolated cases, no effect was noted even after three or four doses. Between these two extremes were observed all types of reactions. The most annoying feature of the technic was an extreme excitability noted in a small number of cases. However, restlessness was usually manifested by only a mild stirring at the height of the uterine contraction, and the patient could be controlled with little difficulty. When excitement was marked and the patient was difficult to restrain, it usually was found necessary to discontinue the medication and substitute nitrous oxide or ether inhalations. If this restlessness was noted early in labor it could easily be controlled with adequate doses of morphine. In the management of each case under this type of treatment an individual consideration of the effect of the drug was found to be essential if satisfactory results were to be obtained.

REPORTS OF CASES

In the last series of 100 cases personal observations were made by the authors and accurate detailed records kept. This does not represent the total number of cases in which the drug was used, but we prefer to report only those cases which we were personally able to follow. In the cases not reported we have reason to believe that the results were consistent with our own. In this reported series observations were made as to the degree of analgesia and amnesia, the effect on the mother and fetus, the average duration of labor, and the various factors which might influence the success or failure of the technic. More recently a number

of cases was studied by means of the hystero-graph to determine the effects, if any, of paraldehyde upon the strength and duration of the uterine contractions.

Detailed records were kept on each patient receiving the treatment. In these, the medication used, the patient's reaction to the drug, the progress of labor, and the details of delivery, were noted. A final analysis was made and the results graded according to the criteria used by Kane. The summary of results is given in Table I.

TABLE I. GENERAL SUMMARY OF RESULTS

100 CASES	EXCELLENT	GOOD	FAIR	POOR
Primiparas	60%	20%	16%	4%
Multiparas	43%	27%	27%	3%
Total	53%	23%	20%	4%

From this, it is seen that the drug was more satisfactory in primiparous labors, in 60 per cent of which the results were all that might be expected. These patients were quiet and objectively free of discomfort, and had absolutely no recollection of labor pains when questioned about this a day or two later. In 20 per cent the results were good and amnesia was complete, although during labor the patients showed varying degrees of discomfort and excitement. In the third group there were 16 per cent who had only partial amnesia and did not seem to be entirely free of discomfort during labor. In the last group, there were 4 per cent, in whom the treatment failed entirely. The better result in primiparas apparently was due to a longer labor and consequently more complete medication. It is seen below that better results were obtained in those patients in whom labor was more prolonged. It is noted also, that in the groups of fair and poor results, the medication was given relatively later in labor than in the other groups.

TABLE II. RESULTS WITH RELATION TO LENGTH OF LABOR

RESULTS	NO. CASES	AVERAGE TOTAL LENGTH OF LABOR		AVERAGE LENGTH OF LABOR AFTER MEDICATION WAS BEGUN	
Excellent	53	22 hours	10 mins.	10 hours	56 mins.
Good	23	19 hours	36 mins.	10 hours	1 min.
Fair	20	14 hours	18 mins.	7 hours	18 mins.
Poor	4	17 hours	4 mins.	8 hours	22 mins.

A summary of the medication used in each of the groups is given below. It will be seen that no supplementary drugs were given in most cases. In this study, medication in addition to paraldehyde was withheld in order to study the action of the drug unaided. However, it is our opinion that many cases would have shown better results had morphine been given more often early in labor.

TABLE III. SUMMARY OF ALL MEDICATION USED

RESULTS	NO. PATIENTS RECEIVING SUPPLEMENTARY MEDICATION			PATIENTS RECEIVING PARALDEHYDE ONLY	
	AV. NO. DOSES PARALDEHYDE	MORPHINE	SOD. AMYTAL	NUMBER	AV. NO. DOSES
Excellent	3.0	12	5	36	2.9
Good	3.0	5	2	16	2.9
Fair	2.5	3	7	10	2.0
Poor	2.5	1	0	3	2.7

The method by which the cases in this series were delivered is of some interest. As is the practice at City Hospital, low forceps frequently were used to terminate labor. As might be supposed, paraldehyde, as any satisfactory analgesic, greatly decreases the patient's voluntary expulsive forces and therefore would tend to prolong the second stage if intervention were not practiced. However, it is quite possible that labor might have terminated spontaneously in a greater number of cases without a greatly protracted period of second stage labor. In this series, 89 patients were delivered by some operative procedure and 11 delivered spontaneously.

TABLE IV. METHOD OF DELIVERY OF 100 CASES

Spontaneous	11
Low forceps	59
Midforceps	12
High Midforceps	1
Breech extraction	4
Bill-Scanzoni maneuver	8
Podalic version and extraction	5

In all the cases in which paraldehyde was used, there were surprisingly few complications which might have been attributed to the medication. There were no maternal deaths and no stillbirths or neonatal deaths. The patients recovered promptly from the effects of the paraldehyde although drowsiness often persisted for a day or two. In all cases the newborn breathed spontaneously or with slight stimulation and seemed to be entirely free from the effects of the drug. It was noted, however, that the odor of paraldehyde persisted upon the breath of the newborn child for several hours. Why the child is entirely unaffected by the drug, when it is present in large enough quantities to be exhaled for a period of hours, has not been explained. As to the possibilities of some remote or delayed effects which paraldehyde may have on the mother or fetus, nothing can be said at this time except that paraldehyde has been generally recognized to be a powerful hypnotic of low toxicity. Experimental work on this phase of the subject will be necessary to guarantee its absolute safety.

STUDIES OF EFFECT UPON UTERINE CONTRACTIONS

One very important factor which must be considered in judging any type of analgesia during labor is the effect which it has upon uterine

contractions and the progress of labor. Obviously, any medication which materially delays or stops the process of delivery must be discarded as unsatisfactory. After some observation, it was noted that paraldehyde momentarily lessened the intensity and duration of the uterine contractions but did not seriously lengthen labor. In order to obtain some substantial proof of this, a number of patients under treatment with paraldehyde were studied by means of the Dodek hystero-graph. In this manner graphic evidence of the uterine contractions was obtained. The apparatus employed was that devised and used by Dodek, at Maternity Hospital in Cleveland, for the purpose of studying the effect upon the uterine contractions of drugs given during labor and upon the postpartum uterus. Contractions are recorded by fixing the apparatus upon the external surface of the abdomen of the patient. The method is quite satisfactory in that it records accurately the frequency, duration, and intensity of the contractions and does not require any vaginal or intrauterine manipulation.

Fig. 1 is a reproduction of one of these records taken upon a multiparous patient before and after she had been given a single dose of

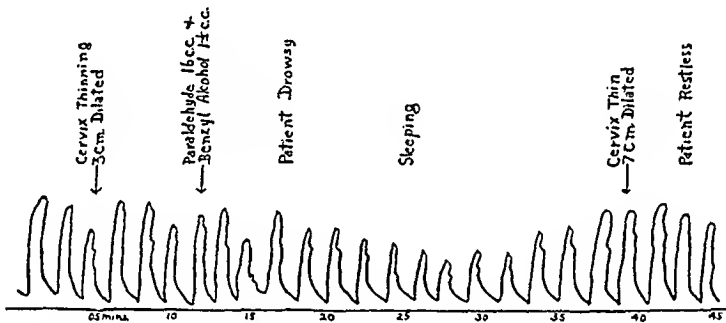


Fig. 1.—Reproduction of a uterine tracing made with the Dodek hystero-graph, showing the effects upon the uterine contraction of a single dose of paraldehyde given rectally. The patient was a multipara in active labor. Note the momentary period of relative uterine inertia followed by a prompt return to normal intensity of the contractions, and the continued progress of labor.

paraldehyde calculated on the basis described above. This illustrates very well the type of response noted in each case. In some, the drug acted less quickly, but almost uniformly there was a lessening of the intensity of the contractions with decreased duration and prolonged interval. However, it will be noted that this reaction was quite brief, and within fifteen or twenty minutes, the contractions regained their previous character. It is quite apparent that the sedative effect secured by the paraldehyde does not depend upon lessening the severity of the uterine contraction, because this desirable action of the drug persists for several hours after the contractions have resumed their previous intensity. In most cases, the contractions became more severe and labor proceeded most rapidly at about the time the maximum hypnotic effect was attained.

Consequently, it seems that paraldehyde given in the manner described does not materially slow labor. The average length of labor

in these cases is shown in Table II. It will be seen that the time elapsing between the beginning of medication and delivery is well within the expected range of normal labors. It must be noted, however, that false labor or uterine contractions which are very feeble may be stopped entirely by paraldehyde as by many other drugs. In order to avoid postponing the onset of labor, the medication always was withheld until there was definite evidence that labor was established. In this matter our judgment was not always correct, but in those cases in which we delayed the onset of labor, we were never led to believe any ill consequences resulted.

DISCUSSION

We are not convinced by our observations that the paraldehyde technic is the ideal method of analgesia for use during labor, but we do believe that it deserves a place among the better procedures. Perhaps further use of the drug will result in such refinement of technic that it will become the method of choice in most cases. Certainly, the use of paraldehyde is not the entire solution to the problem. It has a most disagreeable odor and, being given rectally, is subject to the uncertainties of this route. It is not satisfactory if the medication is begun late in labor, and therefore does not entirely replace the established methods of ether or gas inhalation. At present we do not use the technic routinely, but prefer to continue with the use of morphine and scopolamine in most cases. We are not led to believe that it is better than the morphine-scopolamine technic, although it is a simpler technic, probably more generally applicable, and more readily adaptable for use in institutions in which the morphine-scopolamine routine is carried out with difficulty.

SUMMARY

1. A study is presented in which paraldehyde was used in 150 cases during labor. The procedure followed is described in detail.
2. In 76 per cent of the last 100 cases in which the drug was used, the results were satisfactory, whereas in 4 per cent the method failed entirely. The results are better in primiparous patients and in those patients in whom the medication was begun early in labor.
3. More satisfactory results are obtained when paraldehyde is supplemented with morphine or sodium amytal.
4. Apparently paraldehyde does not materially slow labor, but soon after it is administered there results a momentary period of relative uterine inertia.
5. As far as is known, paraldehyde is absolutely safe in the dosage recommended. It seems to have no bad effects upon the mother or fetus. In this series there were no maternal or neonatal deaths from any cause.

6. Complete approval and recommendation of the technic is withheld until more clinical experience has accumulated.

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QUANTITATIVE FRIEDMAN TEST IN HYDATIDIFORM MOLE AND VOMITING OF PREGNANCY*

PRELIMINARY REPORT

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THE study, herein reported, was undertaken to determine the minimum amounts of urine, at various stages of pregnancy, required to produce positive Friedman reactions. With such normal standards established, a quantitative Friedman test is made available. Such a test would seem to be especially important in differentiating normal pregnancy from hydatidiform mole.

TECHNIC

Nonpregnant does weighing at least 1,500 gm. and between sixteen and eighteen weeks of age were used. All animals were of the same or similar breeds and were obtained from the same source. Fractional intravenous injections of known pregnancy urines were made in dilutions of 0.025 c.c.; 0.05 c.c.; 0.1 c.c.; 0.5 c.c.; 1.0 c.c.; 3.0 c.c.; etc. Two to six rabbits were used for each test. The animals were laparotomized forty-eight hours after the injections. Corpora hemorrhagica or fresh corpora lutea were the criteria for a positive reaction.

STANDARDS

There was a considerable variation in the amount of urine required in individual cases and in the different stages of pregnancy. Concentration of the urine as evidenced by the specific gravity was also a factor to be considered. In general, the smallest amounts gave positive reactions between the sixth and tenth weeks of pregnancy.

Sixty-seven quantitative determinations were made on 41 known pregnant patients. The average minimum amounts of urine giving positive reactions are tabulated in Table II. Further work may alter this table somewhat, but it is felt that there will be no major changes. The smallest amount that gave a positive reaction in normal pregnancy was 0.05 c.c. The maximum amounts varied between 3 c.c. and 5 c.c.

*Aided by a grant from the Hendricks Research Fund.

This latter statement, however, is open to qualifications. The fact that we encounter approximately 2.5 per cent negative errors in our clinical tests (employing 15 c.c. of urine) would seem to indicate that a certain few individuals excrete very little of the substance responsible for the reaction. This, however, does not detract from the use of the test in differentiating hydatidiform mole from normal pregnancy, since we are essentially interested in the hyper- rather than the hypoexcretion of the substance.

HYDATIDIFORM MOLE AND CHORIONEPITHELIOMA

The results of the quantitative test in four cases of hydatidiform mole and one of chorionepithelioma are, likewise, listed in Table II. A wide variation (between 0.0063 c.c. and 5.0 c.c.) is noted in the mole cases. It is most interesting to note that the cases showing marked hyperexcretion of the substance responsible for the reaction (Moles 2 and 4) exhibited typical textbook specimens of hydatidiform mole, i.e., grape-

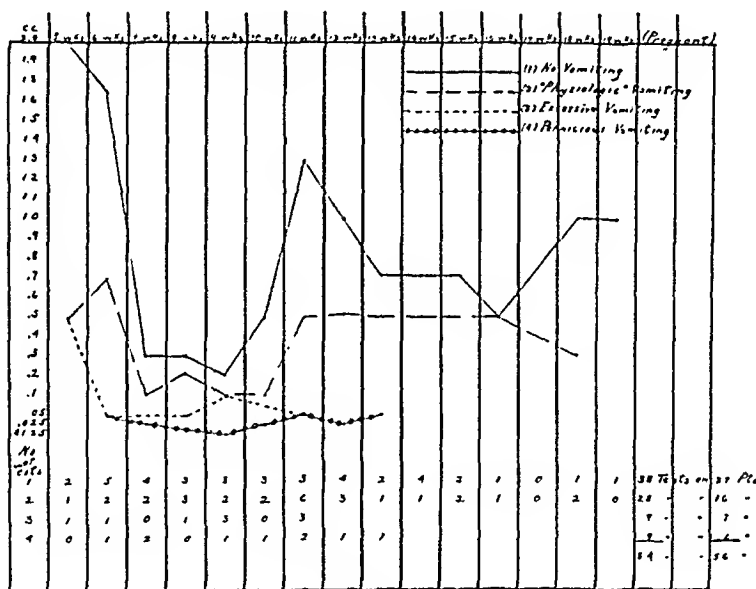


Fig. 1.

like masses of vesicles, whereas, in the other two instances (Moles 1 and 3), the specimens were made up principally of fibrous tissue with comparatively few vesicles.

VOMITING OF PREGNANCY

Early in this study, we obtained a positive reaction with 0.025 c.c. of urine from a patient with pernicious vomiting of pregnancy. The first interpretation placed on this finding was that there was an excessive amount of the substance present due to simple concentration of the urine associated with dehydration. Further study, however, seems to make this simple explanation questionable.

Fig. 1 shows the composite results of 84 quantitative tests on 56 pregnant patients. All these individuals were closely observed clinically. The patients were divided into four groups: Group 1, women

absolutely free from nausea and vomiting. Group 2, patients with some nausea and occasional vomiting, the so-called "physiologic vomiting" of pregnancy. Group 3, patients with an excessive amount of vomiting, some loss of weight, etc. Group 4, definite pernicious vomiting of pregnancy.

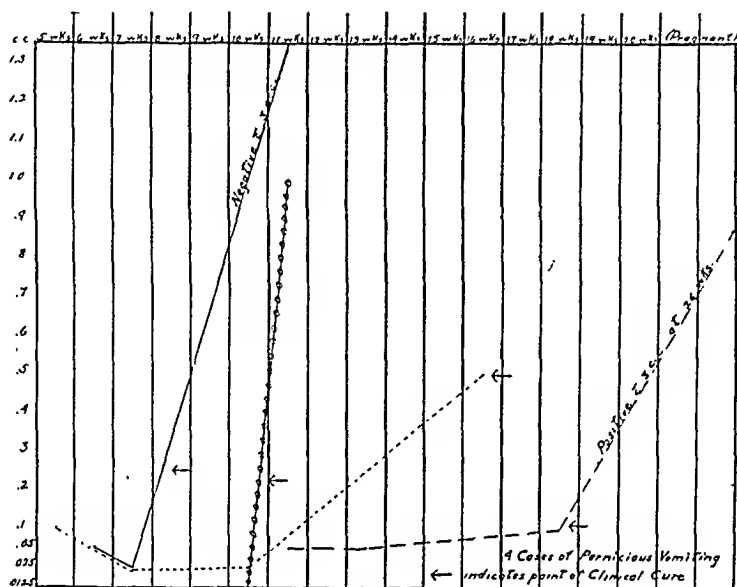


Fig. 2.

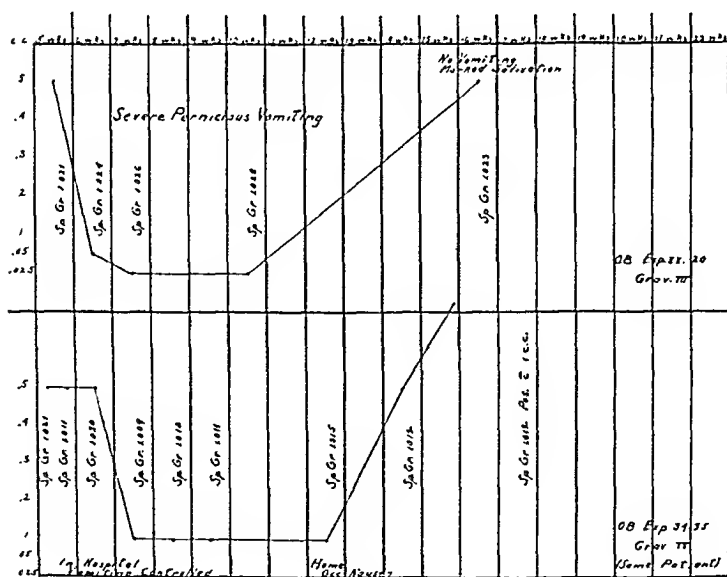


Fig. 3.

Examination of this chart shows that the group in which nausea and vomiting were absent required more urine to produce positive results than did the groups in which these symptoms were present. The contrast is especially marked between the first group and that including the pernicious vomiting cases.

It was further ascertained that in the pernicious vomiting cases, as the symptoms abated, the amount of urine required to produce a positive reaction increased. Fig. 2 shows four of these cases, the arrow in each instance indicating the point at which the patient was considered cured.

Fig. 3 shows a very interesting contrast. The upper portion of the chart represents the quantitative tests on a gravida iii with severe pernicious vomiting. This same patient became pregnant again the following year. She was hospitalized in the fifth week of pregnancy. On a strict régime, pernicious vomiting did not recur, and the lower portion of the chart shows the quantitative studies in that pregnancy.

Fig. 4 illustrates a weekly quantitative study of a patient with the so-called physiologic type of vomiting (Group 2). It will be noted that

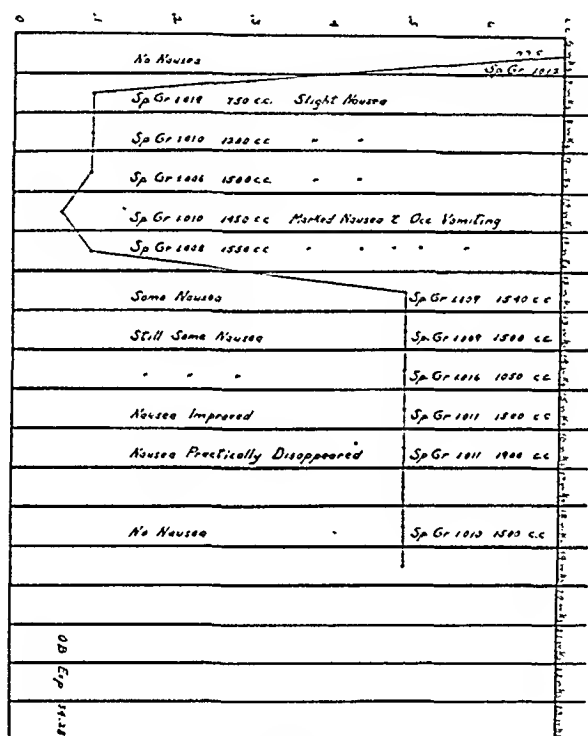


Fig. 4.

in general the periods of nausea were associated with high dilution positive tests. It was observed that while there was no change in the amount of urine required from the thirteenth to the nineteenth weeks

TABLE I

Normal pregnancy	6 weeks	Sp. Gr. 1.018	Pos. with 1.0 c.c.
Pernicious vomiting	6 weeks	Sp. Gr. 1.018	Pos. with 0.0125 c.c.
Normal pregnancy	7 weeks	Sp. Gr. 1.030	Pos. with 0.5 c.c.
Pernicious vomiting	7 weeks	Sp. Gr. 1.026	Pos. with 0.025 c.c.
Pernicious vomiting	7 weeks	Sp. Gr. 1.015	Pos. with 0.025 c.c.
Normal pregnancy	9 weeks	Sp. Gr. 1.019	Pos. with 0.5 c.c.
Pernicious vomiting	9 weeks	Sp. Gr. 1.012	Pos. with 0.0125 c.c.
Normal pregnancy	11 weeks	Sp. Gr. 1.015	Pos. with 1.0 c.c.
Pernicious vomiting with hydat. mole	11 weeks	Sp. Gr. 1.001	Pos. with 0.0075 c.c.

of pregnancy, the intensity of the test, as evinced by "blood points" or fresh corpora lutea in the ovaries of the test animal, definitely decreased. This series of tests was carried out on twenty-four-hour specimens.

Although concentration of the urine, due to dehydration, in the vomiting cases cannot absolutely be ruled out as a factor in the above findings, the following contrasts (Table I) are given to show that simple concentration does not seem to be the entire explanation.

SUMMARY

We are attempting to establish standards as a basis for a quantitative Friedman test. Using these standards, a differential diagnosis between normal pregnancy and hydatidiform mole was attempted in four cases. In two of the moles, definite evidence of a markedly excessive excretion of the substance responsible for the reaction was found. In the other two, such findings were not present. These latter moles did not present the typical pathologic picture; they probably had ceased to grow, or were actually undergoing degeneration. It is our impression, at the present, that the quantitative test, herein described, will be of real value in aiding the diagnosis of an active hydatidiform mole, but that it will be of questionable value in ruling out a mole that has ceased to grow or is undergoing degeneration. The single case of chorionepithelioma does not allow an expression of opinion.

The data presented on vomiting of pregnancy would seem to open a new avenue of approach to a possible etiologic explanation of the condition. The presence of an excessive amount of the substance responsible for the reaction in the urine of vomiting cases has been consistent and has been quite constant as to contrast with the findings in normal pregnancy. The factor of concentration of the urine due to dehydration must, of course, be ruled out. We feel that we are able to eliminate this factor, at least as far as relationship to specific gravity of the urine is concerned. As another link in the chain, we are at present repeating the work as outlined above on blood serum.

While there is insufficient evidence to advance a hormonal explanation of the cause of vomiting of pregnancy, the evidence, to date, would seem important enough to warrant continued investigation.

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THE USE OF PROGESTERONE IN COMBATING HABITUAL ABORTION*

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HABITUAL abortion'' is used in the title of this report in deference to current terminology. "Repeated spontaneous abortion" describes the condition without admitting failure in diagnosis by dismissing it as simply a habit. As investigation in the field of endocrinology advances, new facts are being brought to light which are certain to reveal many hitherto unknown causes of bodily dysfunction. When it was learned that the presence of an adequate amount of progesterone is essential to the nidation and growth of the fertilized ovum in the endometrium, the reason for one type of abortion was automatically explained. When it was realized that lack of progesterone could be responsible for abortion in the absence of physically demonstrable pathology, the method of treatment was obvious. The problem then became one of obtaining progesterone with which to augment the insufficient supply furnished by the glands of the would-be mother. The most commonly available source of the hormone was the extract of the corpus luteum. This complex substance contains antagonistic estrin, and its effect, therefore, could not always be foretold. For several years corpus luteum extract has been employed with marked success in treating spontaneous abortions of undiscovered origin, and with the isolation and commercial availability of pure progesterone, the small percentage of failures should still further be diminished.

The first report of the treatment of habitual abortion by hypodermic injections of corpus luteum extract was that of J. C. Hirst in 1918. Among the patients to whom Hirst was giving this substance for the control of hyperemesis were two who had had 9 and 10 spontaneous abortions, respectively. To his surprise, both of these women carried their pregnancies to term. The suggestion that this method of treatment be adopted in such cases was not widely accepted, although it has been employed with some success by Mazer and Goldstein. In a previous article, the author reported 26 cases of habitual abortion treated as suggested by Mazer and Goldstein, in which 22 living children were obtained. These are included in this report. Krohn, Falls, and Lackner, in 1935, reported 19 cases of threatened and habitual abortion treated by isolated lutein hormone, with successful results in 14.

*Read at the meeting of the Section on Medical Sciences of the American Association for the Advancement of Science held at St. Louis, Jan. 2, 1936.

The 40 cases here reported are all private patients of the social and financial strata from which the obstetric specialist draws his practice. Cases of threatened abortion and those who presented any demonstrable pelvic pathology have not been included in this series. In 20 cases there had been but one previous abortion, and undoubtedly some of these patients would have gone to term without treatment in a subsequent pregnancy. A careful search of the literature failed to provide any information as to the expectancy of successful pregnancy following spontaneous abortion, and as all of these patients had aborted from causes unknown, it is assumed that endocrinopathy was responsible. In 14 cases there had been 2 previous abortions; in 4 cases, 3; in 1 case, 4; and in 1 case, 6. Ten patients had each borne a living child and subsequently had aborted from 1 to 3 times.

Of the four failures previously reported, one pregnancy ended at the sixth month by premature separation of the placenta. In one case, what was apparently a two months' fetus was expelled at the end of the fifth month after three months of treatment. Two patients aborted at the third and fourth months, respectively, after two months of treatment.

Believing that the thyroid gland plays a part in all endocrine dysfunction, and that it stimulates glandular activity in general, thyroid and iodine preparations are given to these patients in addition to progesterone, as suggested by Mazer and Goldstein. Treatment is begun as soon as the patient presents herself for prenatal care, usually after the second period has been missed. Progesterone, in the form of proluton, $\frac{1}{25}$ rat unit, is given intramuscularly every other day for ten doses. This procedure is repeated at three-week intervals until the end of the fourth month. In addition, the patient takes 0.5 gr. of desiccated thyroid three times daily for two weeks and 4 gr. of sodium iodide three times daily for the following two weeks; then, resuming the thyroid, a change is made to sodium iodide every two weeks. At the end of the sixth month, this medication is stopped. The patient's activities are not curtailed except in regard to intercourse, which is forbidden. In the first 26 cases, 2 c.e. of corpus luteum were given instead of progesterone.

During the observation of these 40 cases, there have developed several subjects interesting for speculation and inviting further investigation. No conclusions can be drawn from so small a series of cases, but the recording, as time goes on, of the results of many observers will lead to valuable information regarding these points.

First, in comparing the results in the use of progesterone with those obtained when corpus luteum extract was employed, it will be seen that there were no failures with the former in 14 cases and 4 failures in 26 cases with the gland extract. In one case, the patient had aborted spontaneously in her first pregnancy, aborted after treatment with corpus luteum in her second pregnancy, and was carried to term in her

third pregnancy, when progesterone was used. Pure progesterone, therefore, would seem from this small amount of evidence, to be the more efficient.

It has been a rather common assumption that a full-term pregnancy following one or more abortions was proof that the maternal endocrine system had become properly adjusted and that the abortion "habit" had been broken. One patient in the corpus luteum series, who had previously aborted three times, became pregnant six months after the birth of her child. Not being particularly anxious to have another baby so soon after the first, she took no treatment, and aborted at the twelfth week. The patient who had had six abortions and one living child, in a subsequent pregnancy delayed reporting for treatment until the tenth week. Progesterone injections were started, but abortion occurred after four doses had been given. This case is not reported as a failure as the treatment was obviously inadequate. These two are the only patients who have become pregnant after having produced living children, and the fact that both aborted suggests, at least, that a full-term pregnancy does not cure the endocrine dysfunction which probably caused the previous abortions.

Demanding serious consideration is the question of the normality of children born of mothers who have previously aborted. In the 36 living children in this series, there was one case of spina bifida, one of pyloric stenosis which required operation, and one case in which there were present imperforate anus, a congenital heart lesion, and mongolism. Three of the mothers who, under treatment, produced normal children had previously borne babies with spina bifida. Several investigators, notably Huntington and Streeter, have shown that a large percentage of aborted fetuses show anatomical defects. These fetal defects have been ascribed to deficient germ plasm, but there must be a reason for such deficiency, and the above results at least point to endocrine dysfunction as the possible underlying cause. It may be that preventing the expulsion of abnormal fetuses in the early months of pregnancy is combating nature's provision for the elimination of the unfit.

Recently the author has begun a study of the hormones in the blood of women who have produced defective children. Three have been examined with the rather significant result that two showed very weak positive estrin reactions, while in the third, estrin was entirely absent. This is a subject that deserves thorough investigation. Should it be found that some of the fetal anomalies are due to a deficiency of estrin or other hormones, prophylaxis and treatment would become relatively simple.

SUMMARY

1. In 40 cases of repeated spontaneous abortion treated by progesterone and thyroid extract, 36 living children were born.

2. Pure progesterone seems to be more effective than the extract of the corpus luteum.

3. The fact that a pregnancy has been successfully completed does not obviate the necessity for treatment in subsequent pregnancies.

4. The incidence of fetal abnormality is high among women who bear children after having previously aborted.

5. Endocrinologic investigation of women who bear defective children may be the means of discovering the cause and providing a method of eliminating this complication of pregnancy.

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1835 EYE STREET, N. W.

INTRAMUSCULAR INJECTION OF VITAMINS A AND D CONCENTRATES DURING PREGNANCY

PRELIMINARY REPORT

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THE purpose of this investigation was to show whether high concentrations of vitamins A and D from fish liver oils in a suitable vehicle for intramuscular injection would provide a satisfactory method for administering these two vitamins in the pregnant individual, who, in many cases, due to gastric intolerance and the disagreeable after-taste of high vitamin-bearing preparations and the finicky palate of the gravid, cannot be expected to consume orally with regularity high vitamin-bearing foods or vitamin A and D preparations.

The chief purpose was to determine whether repeated injections at monthly intervals of high concentrations of the fat soluble vitamins would produce untoward toxic effects and whether or not preparation would be assimilated. A blood serum calcium estimation was made on all patients, in order to determine whether the high vitamin intake would produce an abnormally high blood serum calcium with a normal diet or a diet high in calcium and phosphorus. An equally important object of the investigation, however, was to determine the effect of the parenteral concentrate on the general condition of the gravid patient during the prenatal period and its noticeable effect on ameliorating,

to some extent, the complications occurring during parturition. The effect of the treatment on lactation and on the infant were noted while both mother and child remained in the hospital.

METHOD

A concentrate of vitamins A and D prepared from cod liver oil was injected at monthly intervals. During the first visit, a general physical examination was made. Blood samples were taken for Wassermann tests and calcium determinations. The teeth were thoroughly examined by a dental hygienist and record made of the dental condition. After the first visit, blood samples were taken from each patient at monthly intervals to note the change, if any, in blood serum calcium in patients of the control and treated groups. Since the examination and treatment prior to parturition were made in the Bridgeport Welfare Clinic and the deliveries were made in St. Vincent's Hospital maternity wards, the obstetrician concerned in the delivery had practically no knowledge of the prenatal treatment of the patient. While it is difficult to establish a vitamin deficiency in the dietary of the clinic patient, the examination of the teeth and general appearance of practically all patients included in this report seemed to indicate a vitamin D deficiency in their diet.

HISTORICAL

The accelerated metabolism, the augmented needs of the maternal organism of the pregnant, the drain by the fetus for its formation and sustenance, and the rôles of vitamins A and D in these functions, as well as the pathology due to the deficiency of the vitamins, are too well recognized by the obstetrician to be discussed in this article. There are, however, pathologic conditions resulting indirectly from vitamin deficiencies during pregnancy and methods of treatment that require further study.

Wolbach and Howe¹ and others have demonstrated the metaplastic alteration in the epithelia in vitamin A deficiencies. It is undoubtedly the keratinization of the epithelia that is responsible for the lowered resistance to infections. Gardner² noted the favorable influence of cod liver oil concentrate in the treatment of leucorrhea of an infectious origin. Complications of pregnancy and delivery due to vitamin deficiency were reported by Gjorgy and others. Stein³ obtained good results with high vitamin A intake in specific urethritis.

Mellanby and Green⁴ advocate vitamin A therapy as a measure against septicemia. They consider it of special significance that puerperal sepsis is primarily an invasion of the epithelium of the generative organs by pathogenic bacteria. The comprehensive investigation of these workers of the effect of vitamin A and D therapy in 550 pregnant women shows a remarkable reduction of morbidity in the vitamin treated patients.

According to Bosworth, Bowditch and Giblin, the calcium demand for the growing fetus is approximately 0.006 gm. per day during the first four months to over 0.6 gm. at term. This alteration in the concentration and distribution of serum calcium in pregnancy and parturition, obviously calls for a supplementation of vitamin D, which is essential in osteologic growth for the child and the correction of the lowered maternal serum calcium due to fetal drain.

Fish liver oils have been found most suitable as a source of vitamins A and D. The odor, taste, and gastric intolerance of these oils have been serious drawbacks, especially in gravid states. The effectiveness of cod liver oil concentrate as an anti-

rachitic agent has been demonstrated by De Sanctis and Craig⁵ and later by Barnes.⁶ Concentrates of fish liver vitamins in tablet or capsule form constitute an improved step forward. Even here, there are innumerable instances of gastric intolerance and disagreeable after-taste, particularly during pregnancy. Furthermore, many clinical instances of impaired intestinal absorption of vitamins have been reported. Bloch⁷ made effective use of parenteral administrations of cod liver oil concentrate in patients having gastrointestinal and hepatic functional disturbances. Blegvad⁸ was successful in treating night blindness and xerosis due to faulty assimilation with parenteral administrations of a preparation having a potency 100 times that of cod liver oil. A diet high in vitamin A had been ineffective during a trial of six weeks in Blegvad's patient. The patient was given 1 c.c. parenterally with rapid absorption and without local inflammation.

Gordon and Titherington⁹ investigated the parenteral administration of vitamin concentrate in 67 tuberculous patients with vitamin deficiencies, and suggest the consideration of the injections when patients are unable to take a standard diet or cannot tolerate the oral administration of cod liver oil or accessory food substances. Gordon and Titherington's patients received daily or three times weekly, subcutaneous or intramuscular (in a few instances) injections of cod liver oil concentrate into the arms (in a few instances into the buttocks). The greatest number of injections in any patient was 57 (in a period of seven weeks). The absorption of the oil was more rapid and complete than is usually noted in oil injections and not more disturbing than when iron and certain other drugs or combinations are employed. These workers state that when considering their laboratory data, "it seems that the utilization of both vitamins A and D is accomplished effectively through subcutaneous administration."

Wilkins and Kramer¹⁰ obtained calcification and improved blood calcium and phosphorus in children by giving intramuscular injections of an ether solution of cod liver oil concentrate.

PREPARATION OF THE CONCENTRATE FOR INTRAMUSCULAR INJECTION

A concentrate was prepared by dissolving a sufficient amount of a cod liver oil extract prepared according to the Marcus process for concentrating vitamins A and D, in neutral sesame oil of high quality. The finished preparation contained 100,000 to 125,000 vitamin A units and approximately 12,500 vitamin D units (U.S.P.X 1934) per c.c.* The preparation was packaged in 5 c.c. serum vials and stoppered with Duprene stoppers. Sterilization was effected by heating the sealed vials for twenty minutes at 101° C. in an autoclave at three twenty-four-hour intervals. Bacteriologic tests showed that this method of sterilization was satisfactory. Biologic tests seemed to show no destruction of vitamin A during the sterilization process.

Rats weighing approximately 75 gm. were found to tolerate as much as 0.7 c.c. of the prepared concentrate when injected intramuscularly. Encapsulated oil was not found to remain in the muscle near the site of injection as reported by Koehne and Mendel¹¹ when cod liver oil-lecithin emulsion was injected. Apparently the unsaponifiable fraction of cod liver oil when dissolved in sesame oil is more readily assimilated than the cod liver oil.

Before parenterally administering the concentrate to pregnant women, twelve normal male adults received injections of 0.5 c.c. into the gluteal area in order to determine whether local reactions would be produced by the vitamin A and D concentrate in sesame oil. No untoward effects resulted from these preliminary injections and in every case a rapid assimilation of the oil injection was apparent.

*The calcium and phosphorus fraction of milk used in this investigation is known as Phos-Cal.

CLINICAL STUDIES

Four groupings were made of 100 pregnant women reporting to the Prenatal Clinic of the City Dispensary. One group of 42 women served as a control; a second group of 27 women were given intramuscular injections of the prepared concentrate of vitamins A and D at four-week intervals; the third group of 25 women received intramuscular injections of 1 c.c. of the prepared concentrate at four-week intervals, plus 1 gram of calcium and 0.585 gm. of phosphorus in protein combination as found in milk, daily; and the fourth group of 6 women, received 1 gm. of calcium and 0.585 gm. of phosphorus in protein combination as found in milk, daily, but none of the parenteral concentrate of vitamins A and D.

With a few exceptions, the general appearance and dental examination of all patients in the above groups seemed to indicate a vitamin D and calcium deficiency. Although most patients were supplied with food by relief agencies, they were of good weight. Physical examinations were made on all patients. Blood samples were taken during the first clinic visit for Wassermann tests and blood serum calcium determinations. The fall and rise in the blood serum calcium was determined, at four-week intervals, in all patients. The intramuscular injections of 1 c.c. of the vitamin concentrate were made at four-week intervals in patients of the second and third groups. The calcium and phosphorus supplements for the third and fourth groups were supplied in palatable lozenge form. Three of these lozenges which were consumed daily contained approximately 1 gm. of calcium and 0.585 gm. of phosphorus in protein combination such as found in milk.* Since all patients reported to the clinic after the fourth month of pregnancy, the greatest number of injections given any patient was four. All injections were made into alternate gluteal areas, using a No. 19-G needle $1\frac{1}{2}$ inches long, while the patient was standing.

With the exception of a comparatively small number of cases of swelling, redness and itching at the site of injection, there were no local or other untoward effects. In most cases where patients had swelling after one injection, it did not occur in the following injections. This seemed to indicate that the method of injection may have been somewhat responsible for the local reaction which in no case lasted longer than three or four days. Practically all patients exhibiting no local muscular resistance to the injection were free from all minor local untoward effects. The application of warm compresses, as suggested by Gordon and Titherington,⁹ seemed to reduce swelling and itching. Apparently, the concentrate was rapidly absorbed and examination of patients on following visits showed no encapsulated oil in the muscle. While the blood serum calcium determinations may show a higher calcium within the normal range in the patients of the groups receiving the vitamin concentrate and the vitamin concentrate plus the calcium and phosphorus fraction of milk, the difference in the calcium levels in the control and treated groups was not sufficient to attribute a noticeable effect from either treatment. These findings seem to confirm the results of other workers, Cantarow,¹² Stewart and Percival,¹³ Coons and Blunt,¹⁴ Mendenhall and Drake,¹⁵ that the blood maintains its serum calcium level at the expense of the calcium deposits in the body when there is a deficiency in the dietary regimen.

CONCLUSIONS

Conclusions cannot be drawn as to the value of the vitamin concentrate injections alone or in combination with the calcium and phosphorus compound during the prenatal period from the number of cases investigated. However, patients having minor complications, such as

*The intramuscular concentrate of vitamins A and D is known as Jectovin.

feelings of listlessness and sensations of oppressiveness, seemed to be relieved after both the vitamin concentrate injections with and without the calcium phosphorus compound (oral) were administered.

Except for the uniform absence of toxic symptoms, hospital records of the parturitions and the stay of the mother and child in the hospital show nothing outstanding that may be concluded from or attributed to the vitamin A and D injections or the calcium administration. The treated groups were practically devoid of the complications usually occurring in a few patients in the number under observation, such as long labor, loss of blood, insufficient lactation, etc.

Apparently the average woman is capable of storing a considerable amount of vitamins A and D, and since the injections of fairly large amounts of these vitamins do not abnormally affect the blood calcium, it is suggested that the intramuscular injections of vitamins A and D be given consideration where oral administration is ineffective or impractical, in cases of fractures, tuberculosis, pregnancy, severe rickets, etc.

RÉSUMÉ

There is an accelerated metabolism in the state of pregnancy. There is an obvious drain by the fetus on the maternal organism. And there is apparently some degree of vitamin A and D deficiency.

With these clinical axioms in mind, an anticipatory therapeutics by the accoucheur is in order.

Absorbability, effectiveness, infrequent administration, and respect for a whimsical palate and an intolerant stomach are the key desiderata in the administration of vitamins A and D in pregnant women.

Intramuscular injection of a high concentrate in 1 c.c. dosages every fortnight has proved practical and safe from every angle.

In this foregoing clinical investigation no morbid phenomena or postpartum pathology existed. It is not alleged that the intramuscular A and D administrations are the source of normalcy in this series of cases. The primary purpose was simply to determine whether a high concentrate of vitamins A and D from fish liver oils can be administered intramuscularly with good effect and without toxic reaction in the gravid, a state so prone to vitamin inadequacy. It has been shown that it can and with little or no local reaction at the site of injection, and with no fear of toxicity.

The advantages accrued are:

- a. The palate and gastrointestinal tract were not goaded into rebellion.
- b. The dosage, 1 c.c.
- c. Frequency, about every two to four weeks.
- d. Multiplied effectiveness.
- e. Patient under vigilance of her attending physician.
- f. Increased storage of these vitamins thus forestalling a deficiency.

Due to lack of space, tables of blood calcium determinations are omitted but are added to the author's reprints.

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FACTORS AFFECTING THE INCIDENCE OF PUERPERAL MORBIDITY*

WITH SPECIAL REFERENCE TO THE EFFECTS OF VAGINAL AND RECTAL EXAMINATIONS PERFORMED DURING LABOR

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IN A recent report of the Public Health Relations Committee of the New York Academy of Medicine, an attempt was made to divide deaths from puerperal sepsis according to the seat of responsibility. There were 75.1 per cent of the total deaths which were considered to be preventable and of these the physician was held responsible for 81.7 per cent. In studying the errors made by the physicians the committee decided that 65.5 per cent were errors of technique and 34.5 per cent were errors of judgment. The question of errors in technique may seem to have only obstetric interest, but when reflected in maternal mortality statistics, it assumes very evident public health importance.

The question of obstetric technique and its relation to maternal morbidity and mortality is not a new one. It is now universally agreed that certain procedures have a very definite effect on incidence of maternal morbidity and mortality. Among these are operative deliveries, lacerations, hemorrhage, long labors, etc. But these opinions are based upon less factual evidence than is apparent from the certainty with which they are held. This, for example, is true with regard to the effect of a properly performed pelvic examination. It is on this very question that a controversy has existed for many years.

In his classic studies on puerperal infections, Ignaz Semmelweis (1818-1865) enunciated his theories of the etiology of this infection. We find in his *Lehre I* "Puerperal fever is caused by the conveyance to the

*This work was done under the direction of Dr. B. P. Watson, Director at Sloane Hospital and Professor of Obstetrics, College of Physicians and Surgeons, Columbia University.

pregnant woman of cadaveric particles through the agency of the examining finger." In addition to the exogenous type of infection he also admits that "in rare instances the decomposed animal organic material which cause childbed fever when absorbed is produced within the patient herself. These are cases of auto-infection and cannot be prevented."

In an attempt to decrease the incidence of exogenous infection as described by Semmelweiss, an aseptic technic was developed for vaginal examinations. Even this advance did not satisfy some obstetricians, for in 1893 they began to advocate the substitution of rectal for vaginal examination during labor. The pioneers in this movement (Reis, Krönig) claimed the following advantages for their method:

1. A correct diagnosis can be made by rectal examination alone. (Krönig.)
2. Rectal examination is an utterly innocuous procedure in labor, whereas vaginal examinations are always potential sources of infection. (Holmes.)
3. The rectum is more movable than the vagina and permits a better study of the bony pelvis. (Pfleiderer.)

The opponents of rectal examination believe that:

1. There is danger of infecting the dilated cervix by forcing the rectovaginal wall into it. (Leigner.)
2. Rectal examination is unreliable, uncertain, and complications of labor are too often overlooked. (Heynemann.)
3. An error of 10 per cent is generally admitted and one cannot recognize a concealed second stage labor. (LaVake.)
4. One can overdo rectals. Too many rectals may injure the delicate mucosa and rough manipulations should be avoided; the thin edematous septum may possibly be punctured. Thrombosis may be encouraged with serious sequelae. (DeLee.)
5. Unsterile technic and a careless attitude make rectals a potential source of infection.

In reviewing the literature one finds that the effect of the use of rectal examination in reducing maternal morbidity has not been uniformly agreed upon. Such authors as Jegge, Guggisberg, Schuster, Perrote, Pankow, Reis, Claye and Mayes have published conflicting reports on this subject. Jegge, for example, found almost twice the incidence of morbidity in patients examined vaginally as in those examined rectally, whereas Reis believes that "There is no difference in the group examined vaginally and rectally," with which opinion Pankow concurs.

The work of many of these investigators, however, is difficult to evaluate because of

1. The lack of an adequate control series.
2. The failure to describe in detail their technic of examination and selection of cases.
3. The varying and often unmentioned criteria of morbidity.

In the following study we have tried to segregate these complicating factors. Our material consisted of:

1. Six hundred and forty-six normal deliveries obtained from the records of Sloane Hospital (Dr. B. P. Watson, Director); after reviewing all their deliveries during 1932-1933 (3,118 in number).

In order to confirm the results obtained from the analysis of the Sloane Hospital cases we continued along the same lines by studying:

2. Three hundred and ninety normal deliveries obtained in similar fashion at Cumberland Hospital (Dr. M. V. Armstrong, Director); after reviewing all their deliveries during 1933-1934 (2,067 in number), and

3. One thousand four hundred and eight deliveries during 1933-1934 at the Madison Park Hospital, Brooklyn (Dr. A. R. Fritz, Director).

In each series a group of normal deliveries was obtained by excluding every case in which a factor existed that might conceivably cause puerperal morbidity. The factors were

1. Operative delivery (forceps, version, cesarean)
2. Perineal wound (laceration of episiotomy)
3. Prolonged labor, prolonged dry labor, premature rupture of membranes
4. Hemorrhage of more than 500 c.c.
5. Breech deliveries, macerated fetuses, twins and monstrosities
6. Extragenital causes of fever (upper respiratory infection, pyuria, mastitis, and several rarer conditions)

At Sloane Hospital the cases found acceptable were divided into white and colored, and into those which had one vaginal examination and those who had none. *The cases thus selected would vary in their morbidity rate only as they would be influenced by the vaginal examinations.* From each case history was taken the peak temperature on the first nine days of the puerperium excluding the first twenty-four hours. These temperatures were then averaged day by day for each group of patients and in this way an artificial temperature curve was constructed for the puerperium of each of the groups of patients at Sloane and Cumberland Hospitals. In addition the morbidity incidences were determined at three arbitrary standard levels: 99.4°, 100°, and 100.4°. Our morbidity standard was as follows: an elevation in temperature to any of these three levels occurring on any two twenty-four-hour periods following delivery, excluding the first twenty-four hours after delivery. By using this method of cross-sectioning our morbidity, we were in a better position to note what effect the vaginal examination had on the incidence of puerperal morbidity and to make a more accurate analysis of our material. These figures form our basis for the conclusions.

From a study of Table I, it is seen that the incidence of morbidity in the colored patients was approximately 28 per cent higher than in the white patients, although no vaginal examination was done. From this same table and Curve II, it is seen that the incidence of morbidity and the average temperature in the white patient is not affected appreciably

by one vaginal examination. Again this same table and Curve III show that the performance of one vaginal examination in a colored patient definitely elevates the average temperature curve and increases the incidence of morbidity by 50 per cent. Finally Curve IV and Table I show how this effect is submerged if the races are grouped instead of being kept separate. This last curve also indicates that the average temperature on the second and third days, following normal delivery, is higher than on any other day during the puerperium.

TABLE I. SLOANE HOSPITAL

MORBIDITY AT THESE LEVELS	WHITE PATIENTS NO VAGINALS	WHITE PATIENTS ONE VAGINAL	COLORED PATIENTS NO VAGINAL	COLORED PATIENTS ONE VAGINAL	ALL PATIENTS NO VAGINALS	ALL PATIENTS ONE VAGINAL
99.4°	45 16.3%	23 18.4%	30 20.9%	19 29.2%	75 17.9%	42 22.1%
100.0°	13 4.7%	5 4.0%	12 8.3%	28 12.3%	25 5.9%	12 6.3%
100.4°	9 3.2%	4 3.2%	9 6.2%	6 9.2%	18 4.3%	10 5.6%
Total cases	275	125	143	65	418	190

These results are in essential accord with those of Williams, who found that "In 5,514 ward patients 26.4 per cent of the blacks had a temperature rise of 100.4° F. on two or more days of the puerperium as contrasted with 14.4 per cent of whites, a ratio of nearly two to one." In attempting to find a cause of this higher incidence of puerperal morbidity in the colored patient, Harris and Brown of Williams' Clinic in Baltimore investigated the bacteriology of 160 cases of puerperal infection. Of these, 113, or 67 per cent, were due to streptococci. Their conclusions were that "Puerperal infection, due to aerobic beta-hemolytic streptococci, is exogenous in origin." . . . "Since this is the type of infection which is in great part responsible for the high maternal mortality in puerperal infection, it seems to us that our figures reinforce the plea for more conservative obstetrics and particularly for the necessity for the limitation of unnecessary vaginal examination and operative interference at the time of labor. Our work shows that in our material gamma, non-hemolytic streptococcal puerperal infections occur approximately five times as frequently in the blacks as in the whites. We believe that it is this type of streptococcus which gives rise to the preponderance of puerperal infection of the black race. Moreover, if this type of streptococcus is frequently harbored in the vagina and cervix during pregnancy, one might expect it to occur more frequently in the black than in the white as a result of lack of cleanliness in the former." Puerperal infection due to the gamma, nonhemolytic streptococcus is probably endogenous in origin in many cases, and in our series was found to occur five times more frequently in the colored than in the white woman.

TABLE II. CUMBERLAND HOSPITAL

MORBIDITY AT THESE LEVELS	WHITE PATIENTS 1 RECTAL	COLORED PATIENTS 1 RECTAL	WHITE PATIENTS 2 TO 5 RECTALS	COLORED PATIENTS 2 TO 5 RECTALS
99.4°	39 25.3%	10 32.0%	91 32.2%	18 35.0%
100.0°	14 9.1%	1 3.2%	29 10.2%	9 17.1%
100.4°	10 6.5%	0	18 6.36%	5 9.4%
Total cases	154	31	283	53

Similar studies were carried on at the Cumberland Hospital, where rectal examinations are routine. There were very few patients that did not have at least one rectal examination during labor; and because of this we were unable to make a comparison between patients examined rectally and those that were not examined. However, Table II with respect to white patients demonstrates that the performance of two or more rectal examinations in the normal labor does not increase the incidence of puerperal morbidity as compared with cases in which only one rectal was done. From our results at Sloane Hospital we suspected that either type of pelvic examination would cause an increase in the puerperal morbidity of the normal colored patients. Although the cases in this group are few in number, the results so far seem to bear out this conclusion. We plan to make a further study of this subject for a future report.

In addition to studying the effect of the rectal examination on puerperal morbidity at Madison Park Hospital, we also studied the effect of first degree and second degree lacerations, episiotomies, and forceps deliveries on the incidence of puerperal morbidity. The standards used for selecting these cases were the same as those previously discussed. A study of Table III indicates that

1. The occurrence of first degree or second degree laceration or the performance of an episiotomy does not cause an appreciable change in the incidence of puerperal morbidity.

2. The performance of a forceps delivery causes a definite increase in puerperal morbidity and midforceps delivery causes a greater increase than low forceps.

3. Similarly as was found at Cumberland Hospital, rectal examinations in themselves caused no appreciable increase in morbidity.

CONCLUSIONS

Our figures suggest that

1. The incidence of puerperal morbidity following normal delivery without a preliminary vaginal examination is higher in the colored patient as compared with the white.

TABLE III. MADISON PARK HOSPITAL

MORBIDITY AT THESE LEVELS	NORMAL CASES	NORMAL CASES EX- CEPT FOR LACERATIONS 1° AND 2° AND EPISIOT- OMIES	MORBIDITY AT	NORMAL CASES	LOW FORCEPS AND LACERA- TIONS	MID- FORCEPS AND LACERA- TIONS	MORBIDITY AT	NORMAL CASES	ONE RECTAL	TWO TO FOUR RECTALS
99.4°	50 14.39%	89 19.60%	99.4°	50 14.39%	46 24.68%	30 42.25%	99.4°	50 14.39%	19 12.28%	55 17.18%
100.0°	16 4.60%	27 5.94%	100.0°	16 4.60%	20 10.52%	10 14.08%	100.0°	16 4.60%	9 5.8%	15 4.67%
100.4°	6 1.72%	9 1.98%	100.4°	6 1.72%	7 3.68%	5 7.04%	100.4°	6 1.72%	4 2.58%	6 1.87%
Total cases	348	454	Total cases	348	190	71	Total cases	348	155	320

2. The performance of one vaginal examination during labor according to the technique described below has no effect on the temperature in the puerperium of the white patient.

3. The performance of one vaginal examination during labor according to the technique described below definitely elevates the incidence of puerperal morbidity in the colored patient.

4. The performance of multiple rectal examinations in either white or colored patients does not increase the incidence of puerperal morbidity.

5. First- or second-degree lacerations or episiotomies have no appreciable effect on the incidence of puerperal morbidity.

6. Forceps delivery definitely increases the incidence of puerperal morbidity.

At the Sloane Hospital, the patient receives a vaginal preparation on admission, consisting of shaving the pubic hair and a soap and water cleansing of the vulva. Vaginal examinations are not routine. When vaginal examinations are done, in cases where abdominal examination was not satisfactory or to determine the progress of labor, the technique employed was the same as that used in actual delivery, i.e., a sterile gown, gloves, drapes, and an iodine preparation of the lower abdomen and vulva. At the actual delivery, one or more vaginal examinations are routine and no more are done until discharge, unless complications arise. Temperatures are taken every four hours, using calibrated thermometers which are left in the mouth for three minutes.

At Cumberland Hospital, a municipal institution which previously had teaching connections, the technique differs in that rectal examinations are done routinely—vaginal examinations are rarely done. The technique is approximately similar, in that mercurochrome, acetone, alcohol, perineal preparation is substituted for iodine at delivery.

At Madison Park Hospital, a private institution, rectal examinations are done more frequently than vaginal examinations and in a few cases both methods of examinations are used. The technique is similar to that above with the exception that tincture of merthiolate is used as a skin preparation and a solution of 2 per cent lysol is at hand for sponging the vulva.

We wish to express our appreciation of the interest taken in this work by Dr. D. A. D'Esopo, Columbia University College of Physicians and Surgeons, Department of Obstetrics and Gynecology.

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A NEW CONCEPT OF SENILE VAGINITIS

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SENILE vaginitis (also termed agglutinative or adhesive vaginitis, chronic atrophic vaginitis, chronic nonspecific vaginitis) has long been a source of concern to the gynecologist. It occurs most commonly in elderly women either during or after the menopause, but is frequently seen in young women who have been castrated by surgery or by radiation. Rarely it occurs in women who are still in the childbearing age, particularly in those who suffer from extreme malnutrition or from chronic debilitating disease.

The clinical picture is distinctly individual. The patient most frequently complains of a profuse, irritating discharge, and of itching and burning in the vagina. Occasionally there is the complaint of tenderness in the vagina and painful coitus. Examination reveals a markedly inflamed vaginal outlet, with a less severe diffuse inflammation of the entire vaginal mucosa. The discharge is usually white and watery, but may be mucopurulent and is very often blood-tinged. The characteristic lesions are punctate excoriations and ulcers of the mucosa which appear as bright red spots against a light red background. This is the picture of the well-advanced case. Frequently there is a distinct inflammatory reaction of the external genitals, occasionally so severe that it gives the impression of an early leucoplakia.

The etiology of this condition has always been obscure. Curtis (1933) and Davis (1933) both state that yeast infection is probably a causative agent, and that old age is a predisposing factor. Crossen (1930) considers a slight uterine discharge and nutritional disturbances of old age to be the factors involved. Polak (1931) and Graves (1929) ascribe it to the withdrawal of the ovarian hormone at the menopause. Most authors simply state that it is one of the effects of senility. Whatever the principal cause, it is certain that in many cases infections and erosions of the cervix contribute to the onset and severity of the symptoms.

The methods of treatment of senile vaginitis have been as varied as is usual in diseases having no specific therapy. In recent years, the injection of ovarian follicular hormone has proved quite effective as a therapeutic agent. According to Davis (1935), injections of 100 rat units of amniotin (Squibb) three times weekly rapidly

restores the vaginal mucosa to the condition typical of active sex life and permits repair of the associated inflammatory changes. After four to eight weeks of treatment, the patients may remain free of symptoms for—as long as six months, even though the mucosa returns to its previous atrophic state within several weeks after the cessation of injections. The chief disadvantages of the above type of therapy lie in its expense, and in the frequency of subcutaneous injections necessary to maintain a normal vaginal mucosa.

It is also well established that vitamin A is an important factor in maintaining a normal structural and functional state of the vaginal epithelium of the monkey (Turner and Loew, 1932), and of the rat (Evans and Bishop, 1922; Aberle, 1933; Mason and Ellison, 1935). As first emphasized by Wolbach and Howe (1925, 1933), and since confirmed by many other investigators, deficiency of vitamin A manifests itself in a metaplasia and keratinization of epithelia throughout the body. Repair is rapid upon restoration of the vitamin, unless retarded by inflammatory changes which sometimes follow the primary epithelial injury. The vaginal epithelium of many mammals appears to be particularly sensitive to lack of this vitamin. Although no definite alterations in the human vaginal mucosa as a result of deficiency of vitamin A have been demonstrated, there is every reason to believe that this vitamin is quite essential for the maintenance of a healthy state of this epithelium.

In view of the evidence cited above, and the frequent occurrence of senile vaginitis in patients whose diet was both limited and poorly balanced, it seemed to us of interest to determine whether administration of vitamin A might prove of value in the treatment of this condition. The results obtained by this inexpensive and simple method of treatment, over a period of more than three years, have been most gratifying.

The studies presented in this report are based upon 50 patients presenting themselves to the Out-Patient Clinic of Vanderbilt University Hospital for treatment of senile vaginitis. Inquiry into the dietary habits of the patients revealed that the majority existed largely upon a diet consisting of toast and coffee for breakfast, thin soup and side meat, corn bread and jam for lunch, some form of pork, plus one or two vegetables for supper. Sweets and desserts were prominent in all the diets. In many instances, distinct lack of desire for butter, eggs, fresh meat and milk was noted. Such diets, obviously low in vitamin A, are peculiar to elderly women. In some patients, chronic digestive disturbances and habitual use of mineral oil were also suggestive of impaired absorption and utilization of vitamin A from the diet.

The usual method of treatment was as follows: after examination and diagnosis in the out-patient clinic, the following treatment was prescribed: cod liver oil, 16 c.c. t. i. d. for one week; 16 c.c. b. i. d. for one week; and then a maintenance dose of 4 c.c. t. i. d. In some instances, the equivalent amount of vitamin A in the form of haliver oil* was given. Some patients were ordered to take cleansing douches of plain tap water, while others received no treatment other than the vitamin A-therapy. At the time vitamin A-therapy was begun the patients were

*We are greatly indebted to Mead Johnson Company, Evansville, Ind., for generous supplies of "haliver oil" used in these studies.

instructed to increase as much as possible their intake of milk, eggs, fresh meat, and butter. As far as could be ascertained, but few of the patients followed these instructions to any great extent.

Of the 50 patients treated, 20 did not make a return visit; 17 were examined at intervals until no symptoms persisted and healing of the vaginal mucosa was complete; and the remaining 13 patients exhibited no symptoms at the last examination and did not return to the clinic (Fig. 1). In approximately one-third of the thirty patients who made return visits, the symptoms disappeared before the end of the first month of treatment. Three-fourths of the patients were symptom-free by the end of the second month, and in only one instance did the symptoms continue as long as four months after A-therapy was begun. The latter patient, who frequently mixed the cod liver oil with mineral oil, required twenty weeks of treatment.

Healing of the mucosa was judged by complete disappearance of excoriations and of inflammation. The average time for complete healing (16 patients) was six weeks, with a minimum of three and a maximum of fourteen weeks. The use of douches in connection with the A-therapy had no significant effect upon the time of disappearance of symptoms, or upon the rapidity of healing of the vaginal

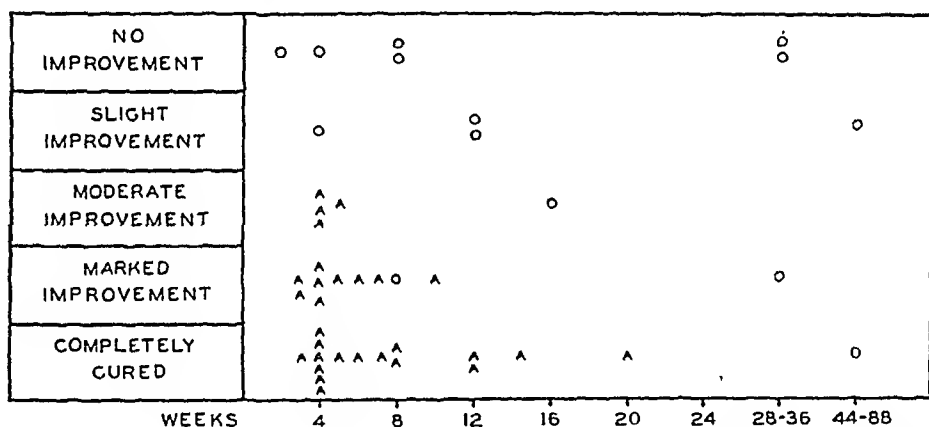


Fig. 1.—Showing the results of treatment of thirty cases of senile vaginitis with vitamin A-administration (indicated by A) as compared with the results of treatment of fourteen cases by the usual topical applications (indicated by O). The symbols indicate the degree of improvement in the patients at the time of their last visit to the clinic.

mucosa. In a limited number of cases reported here, vaginal smears made according to the method of Papanicolaou (1933) at intervals during treatment showed a marked decrease in the relative number of cornified epithelial cells and a much more normal appearance of the nucleated epithelial cells as the condition improved. Biopsies of the vaginal epithelium were obtained from one patient at bi-weekly intervals. As the disappearance of symptoms and healing of the mucosa progressed, there was marked histologic improvement in the epithelium and underlying connective tissue. The rapidity and completeness of the vaginal repair effected by A-therapy, as compared with that induced by other types of treatment (Fig. 1), offer a striking demonstration of the therapeutic value of vitamin A in the treatment of senile vaginitis.

The recent studies of Jeans and Zentmire (1934), Jeans and Zentmire (1934) and Blackfan and Wolbach (1933) indicate that a relatively large number of children are existing upon an inadequate intake of vitamin A quite insufficient to produce any readily recognized symptoms characteristic of the deficiency disease. The present studies indicate that a similar condition may not be uncommon in older women, due largely to inadequacy and to idiosyncrasy of diet. They also indicate that relatively

mild prolonged deficiency of vitamin A may be a very important factor in the etiology of senile vaginitis. Certainly, the improved state of the vaginal epithelium following vitamin A-therapy is a major factor in repair of this condition, regardless of whether other etiologic agents are involved in its production. It should be mentioned, however, that the beneficial effects of A-therapy such as mentioned above can be expected only in instances where the epithelial tissues are already suffering from an inadequate supply of vitamin A, for there is no indication that excess of vitamin A can benefit epithelia receiving an adequate supply of this factor.

It is of interest that the treatment of gonococcal infections has been greatly enhanced by administration of vitamin A (Stein, 1933) and by ovarian hormone administration (Lewis, 1933). The effectiveness of these two therapeutic methods in the treatment of senile vaginitis, as demonstrated by the observations presented in this paper and by those of Davis (1935), affords an interesting parallel. The explanation would appear to lie in the indispensability of vitamin A, and of ovarian hormone, in the maintenance of a normal structural and functional state of the vaginal epithelium.

In summary, this report offers evidence that in 30 cases of senile vaginitis observed, an increased intake of vitamin A, in the form of cod liver oil or haliver oil, proved unusually effective in producing rapid relief of the symptoms and in gross and histologic repair of the vaginal lining. We attribute these effects to the beneficial action of vitamin A in restoring the vaginal epithelium, suffering from a chronic low-grade deficiency of this vitamin, to a normal healthy state.

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Every obstetrician has observed accidents to both mother and child following the injection of posterior pituitary substance during labor. The author therefore cautions against using doses larger than 2 International units at any one time. Furthermore, this substance should only be used in cases of uterine inertia. If these two conditions are observed, pituitary substance will be found to be harmless even in cases of dystocia.

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THE EVALUATION OF THE HYPOPHYSEAL FACTOR IN THE INTERPRETATION OF ENDOMETRIAL CHANGES

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THE introduction of an efficient and practical method of endometrial biopsy^{2, 11} has focused attention on the interpretation of endometrial morphology in terms of ovarian function. This ovarian function is controlled by the underlying endocrine activity, so that the endometrium furnishes an easily accessible tissue which by careful histologic study becomes a valuable indicator of the general endocrine state. It is hoped that this histologic analysis can be expanded to replace laborious and often inaccurate bio-assays of blood and urine factors* which are now used.

Our own interest in this field has been concerned largely with the condition generally known as "glandular cystic hyperplasia of the endometrium." This subject has recently been reviewed elsewhere² and only those phases of the problem related to this study need be considered.

Hofbauer⁹ was the first to produce the condition experimentally. Both normal and spayed guinea pigs were used. These were injected with an alkaline extract of the anterior hypophyses of beeves, prepared according to Evans' method,⁵ or were implanted with bits of beef hypophysis. In normal animals so treated, the endometrium was similar to that seen in human beings suffering from glandular cystic hyperplasia. In the spayed group Hofbauer found that there was a proliferation of the basal layer of the endometrium and concludes: "Our observations, however, indicate that the internal secretion of the ovary is essential for the changes occurring in the upper part of the uterine mucosa—the 'functionalis' while the basal layer is under the control of the anterior pituitary lobe as judged by the response of this structure to repeated pituitary administration in ovariectomized animals." Hofbauer's experiments have been confirmed by Chilese⁴ who found even more marked endometrial reactions after pituitary administration in the spayed animal.

In a paper published shortly after Hofbauer's contribution Burch, Williams and Cunningham,³ viewing the problem from the then apparently well-established absence of any direct action of the hypophysis on the endometrium, considered that the hypophyseal action was mediated through the ovary. They concluded that endometrial changes are the result of the action of ovarian hormones; that these hormones affect the endometrium in a recognizably different way, and that glandular cystic hyperplasia is the result of an ovarian dyscrasia in which a relative excess of estrin is produced. This latter conclusion was tested experimentally by Wolfe, Campbell and Burch.¹⁸ They successfully reproduced the condition in a large series

*Estrogenic and gonadotropic factors.

of spayed rats and guinea pigs by repeated estrin injections. Their experiments have been repeated and their observations confirmed in the mouse by Parkes,¹² in the guinea pig by Tietze,¹⁷ in the monkey by Zuckerman and Morse,¹⁹ and in the human being by Kaufmann.¹⁰

There are thus two views to be considered in the interpretation of endometrial activity in terms of underlying endocrine function. In one the endometrium is thought to be directly influenced by the hormones of both the hypophysis and the ovary. In the other it is considered to be influenced directly only by the ovary; the activity of the ovary being in turn controlled by the hypophysis. There is considerable support to be found for both in the literature. In support of the view of direct hypophyseal action Shaw¹⁴ states in discussing endometrial hyperplasia: "It is difficult to believe that the stimulus is exerted by the ovaries for the latter are relatively inactive. The uterine hyperplasia is controlled by some other factor reaching the uterus independently of the ovaries." The observation of Hartman, Firor and Geiling⁷ that menstruation fails to appear after the cessation of estrin injections in the hypophysectomized monkey has led to the belief that the anterior hypophysis elaborates a specific menstrual hormone which acts directly on the endometrium. On the other hand, the absence of any direct hypophyseal action on the endometrium is indicated by the work of Smith,¹⁶ who found no essential difference in the response of the reproductive tracts of ovariectomized and hypophysectomized rats to follicular hormone. Hill and Parkes,⁸ likewise, found no difference in the response of the endometrium of the ovariectomized and the hypophysectomized ferret to follicular hormone. Further, Robson,¹³ in studying the bleeding which follows cessation of estrin injections in the bitch, states that this bleeding is not abolished by hypophysectomy.

The issues raised by these divergent findings have such an important bearing on the practical evaluation of endometrial changes that it has seemed worth while to examine the question experimentally. Therefore, six spayed guinea pigs were injected every day for fourteen days with 1 c.c. of an alkaline extract of the anterior hypophysis prepared according to Evans' method.⁵ Eight noninjected castrates served as controls. In the control, or noninjected series, the surface epithelium was low cuboidal, there were no mitoses, the glands were collapsed and the stroma was thin (Fig. 1). In the injected animals, the surface epithelium consisted of one to two layers of tall columnar cells. Occasional mitoses were observed. There was some glandular dilatation and the stroma was definitely more compact than in the controls. There was, as Hofbauer and Chilese had reported, a definite and unmistakable reaction (Fig. 2). It was, however, far less intense than that observed after injection of small amounts of estrin (compare Figs. 2 and 6). Since it was similar in type to the hyperplasia produced by small doses of estrin and since Brouha and Simonnet¹ have demonstrated that the hypophysis



Fig. 1.—Uterus of Guinea Pig 182. This animal had been castrated for two weeks. $\times 200$.

Fig. 2.—Uterus of Guinea Pig 191. This animal received 1 c.c. of beef pituitary extract prepared according to Evans' method daily for fourteen days. $\times 200$.

Fig. 3.—Uterus of Guinea Pig 127. This animal received comparable amounts of the water soluble ether extract made from Evans' extract after boiling and autoclaving. $\times 200$.

Fig. 4.—Uterus of Guinea Pig 129. This animal received 1 c.c. of boiled parturient urine daily for twenty-one days following complete hypophysectomy and castration. $\times 200$.

Fig. 5.—Uterus of Guinea Pig 125. This animal received 1 c.c. of boiled parturient urine daily for twenty-one days following partial hypophysectomy and castration. $\times 200$.

Fig. 6.—Uterus of Guinea Pig 198. This animal received 1 c.c. of boiled parturient urine daily for twenty-one days after castration. $\times 200$.

contains a small amount of estrin, it was determined to see if the estrin content of the anterior hypophysis could be sufficient to give a reaction of the degree seen in the injected animals.

The alkaline extract was acidified by the addition of 15 c.c. of concentrated hydrochloric acid to each 100 c.c. of the extract. This acidified extract was placed in an autoclave at 15 pounds pressure for two hours, in order to liberate the combined estrin and to destroy the gonadotropic activity of the anterior pituitary hormones. The material was then thoroughly extracted with ether, which was evaporated on a water-bath. The residue was taken up in enough physiologic saline to make a volume of this solution equivalent to a volume of the original extract. The material was tested for gonadotropic activity on the ovaries of infantile mice and of hypophysectomized rats. All tests were negative.* It was then injected into a series of nine spayed guinea pigs; the amount of material injected and the duration of the experiment were the same as in the former series. The reaction in these animals was uniformly more intense than that produced by the untreated extract (Fig. 3). It would seem, therefore, that the endometrial changes observed in spayed animals after injections of an alkaline extract of anterior hypophysis may be due to the estrin present in the extract rather than to hypophyseal hormones.

The experiments, while enlightening, do not completely exclude the concurrence of the anterior hypophysis of the test animals in the production of the reactions noted, or the action of some as yet unknown hypophyseal factor which might occur in pathologic conditions such as glandular cystic hyperplasia. It was therefore decided to attempt the experimental production of this condition in hypophysectomized animals.

In a previous series of experiments,¹⁵ we had seen that the injection of 1 c.c. of parturient urine, which had been repeatedly boiled, would produce a well-marked glandular cystic hyperplasia of the endometrium of the spayed guinea pig. This dosage of the same urine was then administered to five hypophysectomized guinea pigs. These animals exhibited well-marked glandular cystic hyperplasia of the endometrium (Fig. 4). Four partially hypophysectomized animals also exhibited well-marked glandular cystic hyperplasia (Fig. 5). When the endometria were compared with those obtained from six similarly treated nonhypophysectomized castrate guinea pigs (Fig. 6), it was seen that the reaction was qualitatively similar in all groups but was quantitatively least in the completely hypophysectomized group and greatest in the nonhypophysectomized group; the partially hypophysectomized group exhibited an endometrial reaction intermediate between these two groups. The difference in sensitivity may well have been due to some general effect of the operative procedure. It is interesting that par-

*According to Evans,⁸ boiling does not destroy the synergistic activity of extracts prepared by this method.

tially hypophysectomized animals are far less fragile than those animals from which the hypophysis has been completely removed. Guinea pigs are very sensitive to hypophysectomy, and one is fortunate to have 15 per cent of the animals to complete an experiment of this kind.

Our purpose in these experiments has been an attempt to evaluate the hypophyseal influence on the endometrium as it may apply to our studies of endometrial tissue obtained from clinical cases. We believe that we have been able to show a rationale for the reports of the production of endometrial hyperplasia by hypophyseal substance, i.e., by its contained estrogenic substances. We have also shown that hyperplasia can be produced experimentally in the absence of the hypophysis by substances known to contain no appreciable amount of hypophyseal hormone. The differences observed in the complete, partial, and non-hypophysectomized animals seem to be of a quantitative nature. They do not exclude the possibility of a sensitization of the endometrium by a hypophyseal element, however, we feel that they are to be explained more logically by the general systemic state of the animals. These studies lend further evidence to the theory that the morphologic changes of the endometrium are influenced directly only by the ovary.

SUMMARY AND CONCLUSIONS

Six spayed guinea pigs received 14 daily injections of 1 c.c. each of an alkaline extract of anterior hypophysis prepared according to Evans' method. The endometria of all showed slight but unmistakable hyperplasia.

An equivalent amount of the same extract after being autoclaved at 15 pounds pressure for two hours and boiled thirty minutes produced a similar reaction in nine spayed guinea pigs. The extract so treated showed no gonadotropic activity.

Endometrial hyperplasia was produced in five completely hypophysectomized and in four partially hypophysectomized spayed guinea pigs by injection of 1 c.c. daily of boiled parturient urine for twenty-one days. These were compared with the nonhypophysectomized castrates similarly treated.

The anterior hypophysis need not be considered as a direct factor in the evaluation of the endometrium from a clinical standpoint.

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THE EFFECTS OF PROGESTIN ON AFTERPAINS*

A PRELIMINARY REPORT

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IN REVIEWING the recent advances in the field of endocrinology, one is impressed with the accumulated experimental data associated with the corpus luteum hormone, progesterin. In view of the vast amount of literature existing, pertaining to the physiology of this hormone, we shall limit our review briefly, only to that work which is relevant to our particular studies. Of all the functions attributed to progesterin, that of inhibiting uterine motility is the one with which we are concerned in this presentation.

Estrus motility in the rabbit has been inhibited, and theelin-produced uterine motility prevented, by progesterin-containing extracts of corpora lutea of swine, as demonstrated by Reynolds and Allen.¹

Knaus,² who uses the excised rabbit's uterus in vitro, finds that corpus luteum extracts inhibit the normal response of uterine muscle to the oxytocic principle of posterior pituitary.

Novak and Reynolds^{3, 4} believe that a disturbance of the normal motility factors of uterine muscle is responsible for the pain of dysmenorrhea in some cases. Theelin is an excitant and progesterin an inhibitor of this motility.

Allen and Reynolds⁵ conclude that the two hormonal effects, endometrial proliferation and inhibition of estrous motility, are attributable to the single hormone, progesterin. They used the crystalline forms of progesterin which were prepared by methods similar to those of Wintersteiner and Allen.⁶

Reynolds⁷ states that "under the influence of estrin, the contractions of the uterus become increasingly coordinated and powerful, in the latter part of gestation. Until this time the hormonal influence of estrin is held in abeyance by virtue of the antagonistic action of the lutein hormone, progesterin, and possibly other hormones (prolan) as well."

Krohn, Falls, and Laekners have obtained successful results with progesterin in the treatment of threatened and habitual abortion. These same investigators⁸ have studied human uterine contractions by inserting a hydrostatic bag into the uterus on the seventh day postpartum. Their observations are indeed enlightening. Normal uterine contractions were completely inhibited in the great majority of cases by one rabbit unit doses of progesterin (eorlutin). The effect became manifest in from

*Read before the Brooklyn Gynecological Society, December 6, 1935.

five to ten minutes and lasted for the entire time (two to three hours) that the tracings were recorded. They were, therefore, unable to state how long this action persisted. In most instances, all motility of the uterus was suspended following the injection of progestin. Pituitrin elicited very little or no response while the uterus was in a state of quiescence from progestin. If progestin was administered during a pituitrin reaction, the contractions disappeared in from ten to twenty minutes. The uterus could not be sensitized to pituitrin with estrogenic hormone during the period in which the uterus was under the influence of progestin.

The foregoing clearly demonstrates the inhibitory action of progestin on uterine motility. It is a disturbance of this motility which obtains in a uterus which is the seat of afterpains. Such a uterus is in a state of increased motility. This is best described by quoting Williams,¹⁰ who states: "In primiparous women the puerperal uterus remains in a state of tonic contraction and retraction, unless it has been subjected to unusual distention, or blood clots or other foreign bodies have been retained in its cavity, as a consequence of which active contractions occur in the effort to expel them. In multiparous women, on the other hand, the uterus has lost part of its initial tonicity, so that persistent contraction and retraction cannot be maintained, and consequently it contracts and relaxes at intervals, the contractions giving rise to painful sensations, which are known as after-pains."

Afterpains may also appear, or if already present, may be accentuated, when the baby is put to breast. This is dependent on a reflex mechanism, stimulating uterine contractions, and resulting in pain.

Therefore, we may assume that afterpains are ultimately produced by increased uterine motility, regardless of the initial cause. Furthermore, we know from the work of the previously cited investigators that progestin is capable of inhibiting uterine contractions. If our assumptions are correct, we should logically expect inhibition of the uterine motility associated with afterpains, through the use of progestin. If this is accomplished, it should be registered in terms of pain-relief following the administration of progestin. This forms the basis of our studies.

In addition, we thought it advisable to record other observations relating to the effect, or lack of effect, on the normal processes of the puerperium by progestin.

We believe, as Polak¹¹ did, that afterpains accomplish a physiologic purpose through the mechanism of their production. We know also that the pain may be nonspecifically relieved by the administration of sedatives, and that it usually disappears by the third or fourth day. Our object, however, is not to introduce a means for the prevention of this condition, but rather to further demonstrate the property of progestin to inhibit uterine motility of a painful nature, in a situation excellently suited for this purpose. If, however, further studies warrant it, progestin may then be accepted clinically as a therapeutic agent where afterpains are concerned.

PROCEDURE AND RESULTS

This study was made on 55 puerperal women with a corresponding number of "controls," all of whom were delivered at Cumberland Hospital from July 1 to Sept. 1, 1935. Only multiparas were chosen, since the occurrence of afterpains in women delivering for the first time is infrequent enough for one to question the diagnosis. In every instance an attempt was made to correlate as closely as possible the patient with her "control" in respect to age, parity, physical condition, duration of labor, and type of delivery.

Although we realize that the number of cases studied is small, yet our results have been so conclusive that we feel a preliminary report is warranted.

In order to be certain that the injection of progestin would have no ill-effects upon the patient, particularly with respect to hemorrhage, an initial group of 16 patients who had passed the fifth day of the puerperium was chosen for observation. Following the example of Falls and his collaborators, we began with the seventh day postpartum and after each injection watched the patient closely for symptoms or signs of frank hemorrhage, cessation of involution, and systemic or local reaction. Finding no harmful results, we next chose six-day cases and then proceeded to the fifth day postpartum, after which we felt reasonably safe in taking up our actual study.

This series, therefore, exclusive of the 16 cases mentioned above, consists of 7 patients who had reached the second day postpartum, 7 the first day, 8 twelve hours, and 17 six hours, respectively, following delivery. All of these cases, totalling 39, to be analyzed below, received 1 c.c. of pituitrin and gynergyn immediately following the third stage of labor, after which no oxytocics were administered. Except in two instances, where the initial dose was repeated, each patient received one rabbit unit of progestin injected deeply into the deltoid muscle.*

In order to avoid any technical error, all the results were checked and tabulated by one of us as follows:

I. *Age and Parity.*—The extremes of age were eighteen and forty-five years. More than 75 per cent of the patients were between the ages of twenty and thirty-five years. The majority had been delivered of at least two children in the past, the lowest being one previous parturition and the highest eleven.

II. *Type of Delivery, Anesthesia and Duration of Labor.*—Only those patients who had delivered spontaneously were selected for study. Nine of these received a light ether anesthesia, the others requiring only appropriate sedatives. The average duration of labor was ten hours, the shortest being two, and the longest fifty-seven hours.

*The progestin was prepared by the method of Allen and Meyer (Am. J. Physiol. 106: 55, 1933), the final product being dissolved in sterile almond oil for injection. The extract was standardized according to the method of Corner and Allen (Am. J. Physiol. 88: 326, 1929).

III. *Red Blood Count and Hemoglobin*.—An accurate red blood count and hemoglobin determination (Darc) was made on each patient and her corresponding control prior to the injection of progestin and again one day before discharge. The average drop in hemoglobin in those receiving progestin was 4 per cent, while that of the control cases was 3.5 per cent. The variation in the number of red blood cells of both the injected and control groups was even less marked.

IV. *Afterpains*.—The degree of pain was judged as mild or severe enough to require sedation. Before selecting the cases, a careful examination was made to exclude any other possible cause of the pain. Only those patients experiencing severe afterpains were utilized.

A. Of our 39 patients, 34, or 87.1 per cent, obviously suffering from severe pains, enjoyed complete and permanent relief in from fifteen to thirty minutes following the injection of one rabbit unit of progestin. In 15 of these, however, occasional discomfort was experienced while the baby was at breast.

There were 5, or 12.9 per cent of failures. Of these, 1 patient had 2 large fibroids which not only prolonged the duration of labor but also markedly delayed involution during the puerperium. In 2 patients there was no relief following the first dose of progestin, given six hours postpartum, but following the administration of another dose (one rabbit unit) six hours later, there was complete disappearance of all pain. In another case the patient presented all the classical symptoms and signs of parametritis on the third day of her puerperium. In the fifth and last case no explanation was found for failure of the progestin.

B. In the control group of 55 cases, only 6 did not suffer any discomfort following delivery. Of the remaining 49 patients, over 40 per cent required 2 or more doses of codeine and acetyl-salicylic acid to obtain relief; 3 patients received morphine sulphate, gr. $\frac{1}{4}$, while the others were more comfortable following the application of an ice bag to the abdomen.

V. *Lochia and Lactation*.—Lochial discharge was classified as scant, moderate, or profuse. There was no significant change in the flow of any patient receiving progestin and no relative difference as compared with the control group.

There was no disturbance in the secretion of milk in any of the patients.

VI. *Involution of the Uterus*.—The distance in centimeters of the fundus from the symphysis was measured daily. In all cases involution proceeded normally as compared with the controls, and in all but one case (complicated by fibroids) the fundus had reached the symphysis by the tenth day.

VII. *Hemorrhage Following Progestin*.—In no case was any actual bleeding detected.

VIII. *Local or Systemic Reaction*.—Two of the patients developed an area of erythema at the site of injection which itched intensely, but subsided in one to two hours without therapy.

One patient complained of headache and a sensation of heat fifteen minutes after the injection of progestin, which soon disappeared without any disturbance of pulse, temperature, or respiration.

DISCUSSION

Our results conform with our original assumption, that the action of progestin on increased uterine motility in the early puerperium should be registered in terms of pain-relief.

Our results show that progestin is capable of completely relieving afterpains in 87.1 per cent of instances by a single injection of one rabbit unit of hormone.

These results raise the question, therefore, as to the mechanism of the action of progestin under the conditions prevailing in our observations. Especially is this so inasmuch as involution of the uterus proceeds unaltered and uterine tone is maintained, following progestin administration in the amounts employed in this work. The studies of Falls and his associates show that on the seventh day postpartum uterine contractions may be completely inhibited by progestin administration under the conditions of their experiments.

Although we did not graphically record uterine contractions, our results demonstrate at least an elimination of those contractions productive of pain, following the administration of progestin.

SUMMARY

We have reported observations showing the complete relief of afterpains in 87.1 per cent of cases by the administration of a single dose (one rabbit unit) of progestin.

Normal processes of the puerperium were unaffected.

We wish to express our appreciation to Dr. William C. Meagher, Director of Obstetrics, Cumberland Hospital, for permitting us to undertake this work, and to Dr. Samuel R. M. Reynolds, at whose suggestion these studies were initiated, for his invaluable advice and criticism.

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ADDENDUM

Since the presentation of this paper, 28 additional patients with afterpains have received similar injections of progestin with complete relief of pain in all but 2 cases, thus making a total of 67 cases treated, with complete relief obtained in 89.6 per cent of these. In this latter group progestin was administered as early as 2 hours after delivery in some instances, with no harmful effects.

RESULTS OF TREATMENT IN PLACENTA PREVIA*

BASED ON A STUDY OF 283 CASES FROM THE JEWISH HOSPITAL OF
BROOKLYN

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PLACENTA previa is an accident affecting the particular pregnancy. If its management is skillful and the integrity of the pelvic organs and their supports maintained, subsequent pregnancies will not be influenced by its previous occurrence. The obstetrician's first duty, therefore, is to safeguard the mother's life and never to risk that life in an attempt to save the unborn baby's life. This means that when a diagnosis of placenta previa is made, the patient must be transferred, whenever possible, to a properly equipped hospital where she will be carefully observed or treated. Once bleeding has occurred, a recurrence of the bleeding is an assured fact and so, if the loss of blood reaches a stage where it may be justly termed threatening, the pregnancy must be terminated; procrastination at this stage is dangerous.

How the individual case is to be handled will be determined by many factors, the more important of which are age, parity, duration of intrauterine life, type of previa, degree of bleeding, and whether or not labor has set in. Taking all possibilities into consideration, the methods of treating placenta previa fall into the following groups:

1. Expectant treatment
2. Introduction of the hydrostatic balloon
3. Balloon followed by version
4. Version with or without extraction
5. Cesarean section

Accouchement forcé and vaginal hysterotomy have no place in the treatment of placenta previa, the former because laceration into the lower uterine segment is likely to occur, the latter because the incision is almost certain to invade the placental site with its danger of more hemorrhage.

A total of 283 cases of placenta previa were handled at our hospital up to Dec. 31, 1934. About thirty additional patients were discharged with the diagnosis of placenta previa; careful scrutiny of these records does not justify their inclusion in this study, as the diagnosis is not established by the facts on hand.

*Read before the Brooklyn Gynecological Society, December 6, 1935.

TABLE I

Total cases	233		100.0%
Primiparas	63		22.3%
Viable	55	(19.5%)	
Nonviable	8	(2.8%)	
Multiparas	220		77.7%
Viable	174	(61.5%)	
Nonviable	46	(16.2%)	
Total viable	229		81.0%
Total nonviable	54		19.0%

TABLE II. TYPE

Central	71
Partial	83
Marginal	129

TABLE III. METHOD OF TREATMENT

Expectant	66	23.3%
Bagging	38	13.4%
Bag and version	46	16.3%
Version	102	36.0%
Cesarean section	31	11.0%
	<hr/> 283	<hr/> 100.0%

TABLE IV. EXPECTANT TREATMENT

Total cases		66	100.0%
Viable		54	81.8%
Primiparas	14		
Multiparas	40		
Nonviable		12	18.2%
Primiparas	1		
Multiparas	11		

These are the cases (Table IV) in which labor had set in prior to or at the time of the onset of bleeding or soon after the onset of bleeding, and in which the loss of blood was not great enough to require any manipulation for its control, and those cases in which simple rupture of the membranes was sufficient to control the hemorrhage. Twenty-three and three-tenths per cent of all the cases were so handled, and these figures approximate quite closely those given by other investigators.

TABLE V. INTRODUCTION OF BALLOON

Total cases		38	100.0%
Viable		30	79.0%
Primiparas	8		
Multiparas	22		
Nonviable		8	21.0%
Primiparas	3		
Multiparas	5		

These are the cases in which the bleeding was sufficient to demand control but not enough to require more drastic interference, the patients with marginal or slightly partial placenta previa, not yet in labor, or those patients in whom the labor had not progressed to the point where Braxton Hicks version could be done with safety. Introduction of the balloon may be extraovular or intraovular; the former has

the advantage of preventing prolapse but causes more separation of the placenta with increasing danger to the baby; the latter permits the presenting part to enter the brim as the balloon is extruded, thus aiding in the control of hemorrhage.

TABLE VI. BALLOON AND VERSION

Total cases		46	100.0%
Viable		35	76.3%
Primiparas	5		
Multiparas	30		
Nonviable		11	23.7%
Primiparas	1		
Multiparas	10		

After the expulsion of the bag the presenting part must be depended upon to control the bleeding; if the labor is not sufficient to force the presenting part into the inlet, Braxton Hicks version is the only other means at our disposal to control the bleeding at this stage. It must be done with care to avoid laceration of the friable cervix, and under no circumstances is the baby to be extracted unless the cervix is fully dilated.

TABLE VII. VERSION

Total cases		102	100.0%
Viable		79	77.5%
Primiparas	7		
Multiparas	72		
Nonviable		23	22.5%
Primiparas	3		
Multiparas	20		

When bleeding demands treatment and the cervix is sufficiently dilated to permit the introduction of two fingers into the lower uterine segment, the Braxton Hicks version should be the method of choice. In the hands of the expert it is safe to say that it does not increase the danger for the mother although it carries with it a high infant mortality.

TABLE VIII. CESAREAN SECTION

Total Cases	31	100.0%
Viable primiparas	19	61.3%
Viable multiparas	12	38.7%

That cesarean section offers the greatest degree of safety for both mother and baby no one will deny. However, we must ever bear in mind that this procedure is never justified when the baby is not viable. In our series we had 54 such cases. Also, we must admit that in a certain number of patients with viable babies the hemorrhages are mild enough to be handled expectantly, or require, at the most, simple rupture of the membranes to control the bleeding. In our series another 54 cases were handled so. This gives us 108 patients or 38.1 per cent in which cesarean section was not considered, and we feel that these figures will hold good for any large series of cases. In 30 other viable cases a Voorhees' bag accomplished all that was required, so we have approximately one-half

of the patients definitely out of the cesarean section category. Last, we feel that the majority of multiparous women with placenta previa are not candidates for this method of treatment. In other words, the percentage of cases in which the cesarean operation may be justifiably considered as a possible method of treatment falls well below the 40 per cent mark. No doubt, in the light of present-day knowledge and experience, some of the patients in the preceding groups would rightfully be subjected to cesarean section, but I can do no more than report the statistics as I find them, taking neither the blame for the early unfavorable results nor the credit for the later good results.

TABLE IX. FETAL STATISTICS

Total births	287	100.0%	1 twin
Live births	154	53.7%	
Stillbirths	133	46.3%	
Nonviable	55		
Gross still births	78	27.2%	
Dead on admission	8		
Our responsibility	70	24.4%	
Add neonatal deaths	17		
Total infant deaths	87	30.3%	

If we exclude from the total births the cases of nonviability and those in which the baby was dead on admission, we find a total birth rate of 224, of which 154 were live births, just short of 70 per cent. The total

TABLE X. NEONATAL DEATHS

TYPE	TREATMENT	AGE	
4 Central	4 Version and extraction	28 Weeks	3
6 Partial	7 Spontaneous	30 Weeks	4
7 Marginal	1 Section	35 Weeks	5
	5 Version and spontaneous	40 Weeks	5

TABLE XI. MATERNAL MORTALITY 5.3 PER CENT

Primiparas	3
Multiparas	12

PARITY	TYPE	TREATMENT	CAUSE OF DEATH	INFANT
Primiparas	Central	Bag, version, extraction	Hemorrhage	Stillborn
Primiparas	Marginal	Bag, version, extraction	Hemorrhage	Stillborn
Primiparas	Partial	Version, spontaneous	Hemorrhage	Stillborn
Multiparas	Partial	Version, extraction	Hemorrhage	Stillborn
Multiparas	Partial	Manual dilatation, version, extraction	Hemorrhage	Stillborn
Multiparas	Central	Bag, spontaneous	Infection (emb.)	Stillborn
Multiparas	Marginal	Version, extraction	Infection	Stillborn
Multiparas	Central	Version, spontaneous	Hemorrhage	Stillborn
Multiparas	Partial	Bag, spontaneous	Hemorrhage	Live
Multiparas	Central	Version, extraction, craniotomy	Hemorrhage	Stillborn
Multiparas	Central	Bag, version, extraction	Hemorrhage	Live
Multiparas	Marginal	Manual dilatation, version, extraction	Hemorrhage	Live
Multiparas	Marginal	Bag, spontaneous	Infection	Live
Multiparas	Central	Version, spontaneous	Hemorrhage	Stillborn
Multiparas	Central	Cesarean section	Infection	Live

infant death rate figured on the same basis would be 38.8 per cent. We admit that cesarean section would have saved a number of these babies, but we must not overlook the fact that a certain number of premature babies will not survive under the best of conditions, and certainly placenta previa is far from the best of conditions.

Fourteen of these deaths occurred in the period from 1907 to 1926; the last death occurred in 1929. During the five-year period 1930 to 1934, inclusive, 82 patients with placenta previa have been delivered without maternal mortality.

SUMMARY

1. In the last trimester of pregnancy, a tentative diagnosis of placenta previa should be made whenever the patient has painless bleeding, and hospitalization is imperative.

2. About 23 per cent of all the patients require little or no interference.

3. Before labor has set in and in the early stage of labor, an intra-ovular bag is the ideal method of controlling hemorrhage and of inducing labor.

4. When the cervix is dilated to the point where two fingers can be introduced, Braxton Hicks version should be the choice.

5. Extraction must never be done before complete dilatation of the cervix; hemorrhage from rupture of the lower uterine segment is fatal.

6. Cesarean section is the procedure of choice in certain well-defined cases but is never justified in the presence of a nonviable fetus.

7. The mother's life is never to be jeopardized in the interest of the unborn child.

8. Blood transfusion should always be available and used whenever indicated, whether before, during, or after labor.

9. Forceful dilatation of the cervix, while it was used in conjunction with other methods of treatment in a few of the earlier cases, is to be mentioned only to be condemned; it has no place in today's obstetrics.

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Eufinger and Schulte: Organic Iodides in the Blood and Their Significance in Normal and Toxic Pregnancy, Arch. f. Gynäk. 152: 478, 1933.

The presence of organic iodides in the blood is directly dependent upon the activity of the thyroid gland. Never found in healthy adults; in pregnancy organic iodides can be found in approximately one-third of all cases and in the majority of women who are suffering from the toxemias of pregnancy. This is especially true for eclampsia. There must, therefore, be some form of thyroid dysfunction in connection with the toxemias, but it is impossible at the present time to correlate these facts definitely.

RALPH A. REIS.

POLYNEURITIS OF PREGNANCY*

A REPORT OF FOUR CASES

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CASE 1.—E. P., aged thirty-seven years, gravida v. Entered the Medical Service of the Orange Memorial Hospital on Dec. 13, 1932.

Chief complaint was that of progressive muscular weakness of lower extremities with general incoordination of the majority of the muscles of the body.

A review of her past medical history revealed that the patient was a premature seven months' baby, weighing three pounds. There was a history of convulsions with the first pregnancy in Scotland. Second pregnancy was apparently normal. Third and fourth pregnancies were also apparently normal except for notation that patient was nervous. She was about three months pregnant when first seen and had been vomiting for two months and in bed for the past month. She was becoming more and more nervous and had been losing weight.

Father living and well. Mother died of heart trouble. No brothers or sisters. Husband living and healthy. Four children living and well. No stillbirths or miscarriages.

Home conditions were unsatisfactory. Patient was worried and unable to get the proper food at times.

Physical examination showed nothing abnormal except for slight tenderness in the epigastrium and in both lower quadrants. A pelvic examination showed the uterus to be enlarged to the size of a three months' pregnancy. No masses or induration was felt. Extremities showed a very coarse tremor of the fingers with athetoid movements. There was marked incoordination of the muscles of the upper and lower extremities with disturbed sense of position, inability to stand or to walk, with marked weakness of all muscular groups. There was tenderness over nerve trunks and a flabbiness of muscles. Knee jerks were four-plus at first and diminished later.

Urinalysis disclosed alkaline reaction; acetone four-plus with a few pus cells. Hemoglobin 75 per cent; erythrocytes 4,280,000; leucocytes 7,500; polymorphonuclears 86 per cent; transitionals 1 per cent; lymphocytes 12 per cent; and eosinophiles 1 per cent. Wassermann negative. Renal function test: plus 7 per cent. Metabolic rate: minus 18.

Diagnosis by the neurologist was amyotrophic lateral sclerosis. Patient was discharged on Jan. 10, 1933, to return to the Pre-Natal Clinic.

My attention was first called to the case when I was consulted as to how to get the patient to the clinic and was told that she had an inenrable nervous disease. I suggested her return to the hospital and the induction of a therapeutic abortion.

Patient came to the hospital again on Jan. 14, 1933, and a therapeutic abortion was induced on Jan. 16, 1933. Patient improved gradually and on discharge, Jan. 31, 1933, was able to walk about her room.

Patient was seen six weeks after discharge at the clinic by a neurologist who reported a positive Romberg; reflexes and gait improving.

*Read before the New York Obstetrical Society, January 14, 1936.

CASE 2.—On April 26, 1935, the same patient was referred to the Maternity Center by the Pre-Natal Clinic of another local hospital. She was admitted to the hospital because of constant vomiting and positive Aschheim-Zondek test. She was given intravenous injections of glucose and remained in the hospital for one week during which time she improved.

When she came to the clinic she was very agitated and nervous. After returning home she remained in bed and was on a high carbohydrate diet. She vomited after each meal. On May 31 she was able to return to the clinic but seemed much exhausted. On June 7 she again returned to the clinic and was given whole blood. No evidence or history of paralysis was mentioned at first, but at times her gait had been peculiar. She still complained of vomiting and dizzy spells and became discouraged with her progress at home and decided to enter the Orange Memorial Hospital on June 25, 1935, where she had previously been treated.

Chief complaint upon entrance at this time was dizziness, weakness in legs, and poor vision. The last menstrual period was February, 1935. There was constant vomiting and the patient had lost 22 pounds in the past seven weeks. During this time her legs became weaker and she stated that when she went to walk she felt as though "her feet were stuck to the ground but that after getting started she could walk all right except for unsteadiness."

She also had many dizzy spells and during these spells she saw clouds of smoke before her eyes and became numb over different parts of the body. She also suffered the sensation of falling down when the dizzy spells occurred. These symptoms were similar to those which she had had during her last pregnancy.

Physical examination at this entrance revealed bilateral papilledema. Pelvic examination showed uterus about the size of a four months' pregnancy. Otherwise general physical examination was normal.

Hemoglobin, 60 per cent; erythrocytes, 3,280,000; leucocytes, 8,400; polymorphonuclears, 84 per cent; lymphocytes 12 per cent; monocytes, 2 per cent; basophiles, 2 per cent; occasional anisocytes. Blood chemistry: urea nitrogen, 11.7 mg.; creatinine, 1.2 mg.; sugar, 76.9 mg.; nonprotein nitrogen, 23.4 mg.; chlorides, 0.68 mg.; calcium, 10.5 mg. per 100 c.c. of blood. Blood Wassermann negative.

Neurologic examination demonstrated no sensory changes; no cranial nerve involvement except bilateral second and right eighth. No Laségue; no Kernig; no nystagmus. Pupils reacted to light and accommodation. Diagnosis made by consulting neurologist was cerebellar disease; suspecting cerebellar neoplasm.

Brain consultant suggested the following: The cerebellar and tract disorders may be in the nature of a sclerosis or other degenerative disorder due to faulty nourishment and avitaminosis if cerebellar tumor can be ruled out. He recommended that treatment of two years ago be repeated with a high vitamin B diet.

A diagnosis of polyneuritis was made by the Obstetrical Staff and treatment instituted with high vitamin B diet.

Spinal tap was done and was apparently normal. Patient improved a little at times but dizziness still persisted. Vomiting was much less.

No evidence of increased intracranial pressure was found. Eyegrounds suggested vascular disease rather than pressure. Patient still unable to stand. In view of previous history and present findings the brain consultant felt that the patient's condition would be improved by termination of pregnancy.

As patient seemed to be gradually getting worse, it was decided to do a therapeutic abortion on July 10, 1935. She still had pains in her legs for several days. Within two weeks following therapeutic abortion patient was out of bed and was not so dizzy. Had only slight headache. Within another week she was beginning

to walk. At the end of three weeks she was feeling well, became more stable every day, and was walking about. She was allowed to go home on Aug. 2, 1935, and continue her convalescence at home. Four days after discharge from the hospital, she was brought back to the clinic for examination and seemed to be improving rapidly.

Follow-up note in Neurological Clinic showed on Oct. 2, 1935, that patient was improving, walks three long blocks and then becomes fatigued. Has an occasional occipital headache, not as frequent nor as severe, attacks of vertigo, objects rotating in front of her from right to left. Believes she is moving to the left. However, this sensation is transient. Walks to the left but not as much as formerly. Patient does not fall any more. Muscle strength is improved, but still fatigues easily. There is no further speech difficulty, no attacks of fainting and no vomiting.

Diagnosis made by neurologist: polyneuritis of pregnancy with possible eighth nerve, vestibular nerve or semicircular canal dysfunction.

Examination by otologist on Jan. 6, 1936, showed that the right eardrum had been practically destroyed since childhood, but she could hear a loud spoken voice. The symptoms of dizziness and falling to the left he believed would clear up in time and that the labyrinthian symptoms are a complication of the polyneuritis.

When seen at home patient looked very well and said she was able to do all of her housework and take care of her family.

CASE 3.—L. C., aged thirty-four years. Patient entered the Orange Memorial Hospital on Nov. 9, 1934, with a history of having vomited daily since July 16, 1934, with exception of last two weeks. She continued very weak and feeble and developed symptoms of psychosis with delirium.

Examination showed a markedly emaciated patient about thirty-four years of age, gravida i. There were marked exophthalmos and marked dehydration. She had a positive Stellwag. Thyroid not palpably enlarged. Heart rate regular but rapid. There was a loud blowing systolic murmur heard over the entire precordium. Marked tenderness with spasm over the entire abdomen, greatest in both lower quadrants. Extremities limp, grossly normal in appearance but with great weakness, and loss of reflexes.

Past history revealed heart trouble of long standing. The urine contained albumin 1+; sugar 2+; trace of acetone; few hyaline and granular casts; and numerous pus cells. Hemoglobin, 75 per cent; erythrocytes, 4,280,000; leucocytes, 11,400; polymorphonuclears, 72 per cent; lymphocytes, 28 per cent. Blood chemistry: urea nitrogen, 13.6; creatinine, 1.1 mg.; sugar, 100 mg.; nonprotein nitrogen, 20 mg.; uric acid, 1.3 mg.; Wassermann negative.

Patient was apparently in very poor physical condition, and although slight improvement was made following intravenous therapy, patient failed.

Patient was put on a high vitamin B diet, but her condition was apparently too serious for it to have any effect. A diagnosis of polyneuritis of pregnancy was made. On November 15 a therapeutic abortion was performed. Patient failed quite rapidly and died on November 21.

Necropsy findings: Nerve tissue showed degeneration and fibrosis. Spinal cord showed considerable round cell infiltration. Thyroid and parathyroid showed no pathologic changes. Clinical diagnosis of polyneuritis of pregnancy was confirmed by these necropsy findings.

This was apparently a hopeless case having progressed too far for any treatment to avail. It showed how serious the condition may become.

CASE 4.—C. K., aged twenty-four years, colored, entered the Orange Memorial Hospital on Nov. 12, 1935, because of pernicious vomiting for about three weeks. She was about two months pregnant. Almost no food or fluids had been retained

for the past two weeks, and she had been confined to bed for the past week. Recently vomitus had been dark as well as her urine. Pulse was rapid and weak. Patient very lethargic. Blood pressure 85/55. No heart murmurs.

Her social background is good. She is unusually well educated.

Examination showed a single girl, twenty-four years of age, well nourished and well developed. The sclera of the eyes were markedly jaundiced. Heart was apparently normal. Pelvic examination showed uterus the size of a two months' pregnancy with marked general tenderness. Reflexes were hypotonic. Urinalysis showed albumin 1+; bile 1+; occasional granular casts and red cells; few pus cells and innumerable epithelium. Hemoglobin, 85 per cent; erythrocytes, 4,100,000; leucocytes, 32,950 and 20,000; polymorphonuclears, 84 per cent; lymphocytes, 14 per cent; mononuclear lymphocytes, 2 per cent. Blood chemistry: urea nitrogen, 13.5 mg.; creatinine, 1.2 mg.; sugar, 181 mg., 121 mg., and 86 mg.; nonprotein nitrogen, 65 mg., 110 mg., and 27 mg.; uric acid, 16 mg., 6.1 mg., and 2.5 mg.; icterus index, 20 mg. and 13 mg. Spinal fluid cell count negative, globulin negative, spinal fluid and blood Wassermann negative; sugar, 76 mg.; colloidal gold negative and pressure, 9 mm.

Patient treated for pernicious vomiting. As she seemed to be failing rapidly daily in spite of treatment, a therapeutic abortion was performed on November 18. Patient continued to vomit, and was in very poor condition requiring intravenous medication. She was apathetic, uncooperative, incoherent, and disoriented.

Patient was given a hypodermoclysis daily. Also a diet rich in vitamin B. Condition gradually improved but patient continued to be mentally disturbed. She was able to sit up out of bed but was unable to stand. Was quite irrational at times, especially at night.

On December 9 she was able to take a step or two with the support of two assistants, but her legs would give out under her. She gradually improved but left the hospital on December 15 against advice to convalesce at home.

Summary of neurologist's report: Hyperactive tendon reflexes in upper extremities with diminished tendon reflexes in lower limbs. Babinski R±. Laségués questionable, abdominals absent. Muscle weakness more marked in lower extremities with diminished tactile and pain sense in lower limbs more marked peripherally. Impression, polyneuritis of pregnancy.

When seen at home on December 26 patient was able to walk about room resting lightly on pieces of furniture.

Ten days later patient had been for a walk holding her mother's arm. The only difficulty she had in walking was in going downstairs.

DISCUSSION

A study of these four cases gives several impressions.

1. Polyneuritis of pregnancy is a serious condition.
2. While it is probably due to a dietary deficiency, especially a lack of vitamin B, it may be caused also by an autointoxication of pregnancy.
3. The nervous symptoms are many and varied and laboratory tests give very little aid to diagnosis. The main symptoms are incoordination of muscles with progressive weakness in the muscles of the lower extremities following excessive vomiting of pregnancy. Mental symptoms are usually present.
4. While there are a few cures reported by the use of a diet rich in vitamin B, the condition is so serious that it seems advisable in cases of any severity to terminate pregnancy as well before nerve degeneration has occurred.
5. The use of vitamin B is advisable as a preventive in cases of pregnancy with much vomiting or malnutrition.

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144 HARRISON STREET

ENDOMETRIOSIS DURING THE FINAL MONTH OF PREGNANCY

MARKED DECIDUAL REACTION ABOUT ENDOMETRIOSIS NODULES IN THE PREPERITONEAL FAT

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DECIDUAL reaction immediately beneath the peritoneal mesothelium of the lower abdomen has been established since the comprehensive review and careful study of the subject by Taussig.⁷ A similar reaction which apparently occurs in embryonal remnants of müllerian tissue of the urogenital apparatus¹ has occasionally been observed in the cervix, the upper vagina and the rectovaginal septum. The occurrence of decidua in the proximity of an ectopic implantation of an ovum has also been observed. Less certain is the proposition that decidua may form in a nonpregnant individual due to peritoneal irritation. That there may occasionally be swelling of stroma cells in ectopic endometrium during the progesterin phase of the menstrual cycle seems likely. However, such changes have not been emphasized or pictured in the literature containing lesions which appear to be ectopic endometrial tissue considered in the numerous contributions on the subject. The above aspects of endometriosis have recently been reviewed by Weller,⁸ and they need not be considered in detail here.

On the other hand the study of widely disseminated fragments of ectopic endometrium stimulated by hormones during a normal pregnancy has received scant attention. Geipel³ noted decidual reaction in the pelvic lymph nodes. In some of the nodes so involved the decidua was arranged about ductlike spaces. He did not designate the lesions as endometriosis of lymph nodes² during pregnancy, an interpretation which today would seem the most probable. Sampson⁵ stated that he has recognized four cases of decidual reaction in endometriosis during pregnancy. One of the pregnancies was ectopic and the other three were associated with a myomatous uteri. Hauffer⁴ studied the tissue from a patient who developed a peritonitis from the invasion of the wall of the upper ileum by an endometrial implant. The woman was pregnant, and there was a marked decidual reaction about the endometrial glands. Schaaning⁶ reported a case of endometriosis with decidual transformation in the ovary of a pregnant woman. From this review it would appear that further study of disseminated fragments of endometrium remote from the implanted fetus would seem advisable. Here we wish to characterize disseminated endometrial implants over a large area and picture the proportions

which the decidual reaction may assume about the glands of the implanted fragments. The gross study was made, and the tissue obtained during a cesarean section at term for histologic study.

CLINICAL REPORT

Mrs. J. R., a primipara, aged forty-one, was admitted to the hospital on November 29 with a history of membranes having ruptured at home. The patient was a well-nourished female, pregnant at full term. A physical examination showed heart and lungs normal. Laboratory findings revealed the urine to be negative for albumin and sugar. The blood pressure was 118/74.

After a fourteen-hour test of labor, a low cesarean section was done because of a contracted funnel type pelvis. On opening the abdomen there was a small amount of straw-colored fluid. There were many shotty tubercle-like lesions in the peritoneum of the lower uterine segment extending anteriorly into the vesicouterine space. These tubercles were diffuse and rather widely separated and found to involve also the peritoneum of the broad ligament laterally with a few scattered over the

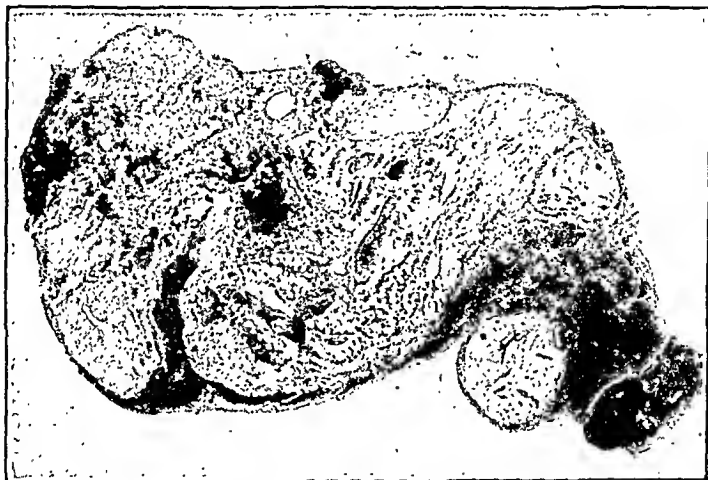


Fig. 1.—Photomicrograph (X20) illustrating the position and frequency of the lesion.

surface of the tubes. The ovaries were of normal size and perfectly smooth. The fimbriae of the tubes were not adherent and the luminae were apparently open. Owing to the escape of blood and amniotic fluid, it was impossible to examine carefully the pouch of Douglas. No tubercles were observed in that region. The uterus showed a thickening of the muscular wall and a rather fibrous consistency with several small intramural leiomyomas in the region of the fundus. A section of the peritoneum over the uterus and that in the bladder flap below was removed for study.

The patient had a normal postpartum course in the hospital and was allowed to go home on the fourteenth day after operation. The abdominal wall healed by primary union. She was examined about six weeks after delivery. A uterus normal in size was found in the anteromid position. The adnexa were normal, and there was no thickening of the rectovaginal septum as elicited by rectovaginal examination. The vaginal vault was normal and the cervix was normal in appearance. The patient appeared in good health, and she had no complaints.

Pathologic Examination: There were three pieces of tissue consisting of peritoneum and preperitoneal fat. One piece appeared to be thin peritoneum in which small gray translucent nodules about 2 mm. in diameter were observed. The

remaining two pieces were of much thickened, grayish white peritoneum which had a considerable amount of hemorrhage in the preperitoneal fat. The histologic examination showed lesions both on and quite deep beneath the peritoneum. The number and position are shown in Fig. 1. The structure of the individual lesion was that of quiescent endometrial glands, surrounded by a wide collar of decidual cells. The cells had large, pale pink staining nucleoli. The pink ectoplasm of adjacent cells fitted closely together, giving the structure a tiled effect. The cells of the endometrial glands varied from low columnar to cuboidal. There had been recent hemorrhage about some of the lesions. There was no somatic reaction to the ectopic endometrium as would be evidenced by old hemorrhage and fibrosis. Curiously enough a few of the endometrial glands had no decidua about them and small nests of decidua, unassociated with endometrial glands, were found throughout the fat.



Fig. 2.

Fig. 2.—Photomicrograph ($\times 200$). Note the wide collars of closely packed decidual cells encircling an endometrial gland.



Fig. 3.

Fig. 3.—Photomicrograph ($\times 1000$). Note flattened cells of an endometrial gland and the large decidual cells.

COMMENT

The patient, a primipara, forty-one years of age had been married eight years. There had been no manipulation which was designed to relieve the eight years of apparent sterility. There had been no operation upon the genital apparatus. No pelvic pathology or misplacement of the internal genitalia suggested interference with normal menstrual physiology. No clinical signs or symptoms suggestive of endometriosis which antedated the pregnancy were elicited. The lack of fibroblastic reaction about and the absence of old blood pigment in the lesions would indicate a rather recent development of the widespread lesions consistent with the duration of the pregnancy.

The lesions appeared to be endometrial in origin. The dissemination was along the route of the uterine lymphatics. Often the location of the lesions was deep in

the preperitoneal fat and did not involve the overlying peritoneal mesothelium. The marked development of decidua paralleled the development of decidua in müllerian stroma rather than the decidual reaction occasioned by the reaction of the peritoneum to female sex hormones or nonspecific irritation of the peritoneum. The above facts indicated endometrial implants spread by the lymphatic route. A regional lymph node was not obtained. The most logical interpretation of these observations would seem to be that the dissemination occurred through the channels of the lymphatics opened by the implantation and growth of a recent ovum.

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A FORTY-NINE-POUND RETROPERITONEAL CYSTIC FIBROID

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I DESIRE to report this case not only because of the large size of the tumor but also because of its peculiar extraperitoneal development and the operative difficulties encountered.

Mrs. E. J. (Fig. 1), aged thirty-six, married, white, presented herself at my office Aug. 20, 1934. She had had an appendectomy for acute gangrenous appendicitis six years before, at which time the surgeon informed her that she "had a fibroid behind the uterus" which he considered inadvisable to remove because of the condition of the appendix. At the same time "a cyst was accidentally ruptured and removed."

Menstruation began at twelve, was always regular, four-weekly, of five days' duration, moderately profuse, and occasionally accompanied by cramps. Her last period occurred August 12. She had been married over fourteen years, had had six induced abortions early in pregnancy, the last nearly thirteen years ago. There had been no pregnancy since.

Since the former operation the patient has noticed progressive enlargement of the abdomen to its present size. Of late she has had considerable abdominal pain and has been practically confined to bed because of the size of the abdomen and extreme discomfort. Except for a slight vaginal discharge and moderate constipation, there have been no pelvic symptoms. At no time has there been meno- or metrorrhagia.

On physical examination the patient did not appear acutely ill but very uncomfortable and severely handicapped by the size of the abdomen. Her weight was 243 pounds. The general examination was essentially negative; heart and lungs were normal; blood pressure was 130 systolic, 95 diastolic; hemoglobin 80 per cent; urine, temperature, pulse, and respiration normal.

The abdomen was huge. The largest circumference was fifty-five and one-half inches and the distance from symphysis to ensiform was twenty-four and three-fourths inches. In the right lower quadrant was the well-healed appendectomy scar. The abdomen contained a large cystic mass and a distinct fluid wave could be elicited.

The vulva and vagina were normal. The cervix was crowded high up behind the symphysis where it could be felt but not seen. The body of the uterus could not be made out, but behind the cervix was the lower pole of a cystic mass which completely

filled the pelvis and abdomen and bulged out the culdesac similar to a large pelvic abscess. A distinct fluid wave was elicited. A preoperative diagnosis of large ovarian cyst was made, and the patient was referred to the Mount Sinai Hospital for operation.

On August 23 the operation was performed under gas ether anesthesia. A seven-inch left paramedian incision was made and the abdomen was opened. The large mass was at once encountered. It felt cystic but did not have the characteristic appearance of the usual large cysts. None of the other abdominal contents could be seen. On manual exploration this mass was found free all around its upper third and also along its right side, except for a few adhesions at the site of the appendectomy, well down into the pelvis where the uterus could be felt. This and the right adnexa were crowded over against the right pelvic wall deep in the pelvis, and the uterus was rotated so that its transverse diameter lay anteroposteriorly. The hand could not be passed down behind the mass below its upper third. It was equally im-



Fig. 1.—Views of patient immediately before operation.

possible to pass the hand between it and the abdominal wall anywhere on the left side between the upper third and the lower pole. The tumor was immovably fixed in the abdomen, and delivery was impossible.

A large trocar was introduced into the tumor directly under the incision, and a little more than three and one-half gallons of port-wine-colored fluid was drawn off. The mass shrank considerably, but its walls were too thick to permit a complete collapse, and it still retained much of its original shape and about one-half of its original size. The adhesions to the right were divided, and the mass was lifted somewhat to the left, exposing the uterus. The right infundibulopelvic and round ligaments were sutured and divided, leaving the right adnexa. The bladder was pushed down, the right uterine vessels were secured and divided, and the cervix was cut across. The left uterine vessels could not be seen, but as they were cut across, the bleeding points were caught and tied. This freed the lower pole of the mass and enabled us to raise it with the uterus from the pelvis and swing it to the left. The distorted anatomic relations were then ascertained (Fig. 2). The tumor arose

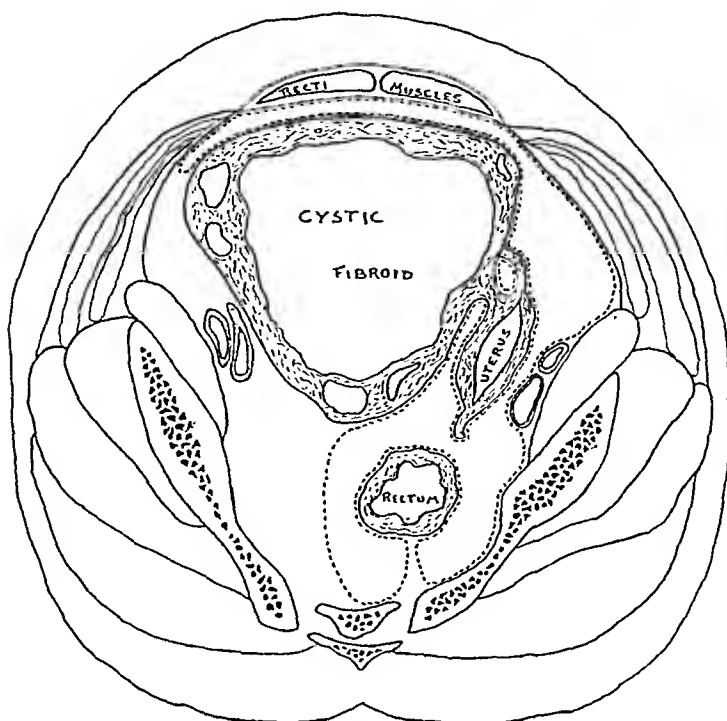


Fig. 2.—Diagrammatic cross-section through the pelvis below the level of the promontory. Peritoneum in dotted lines.

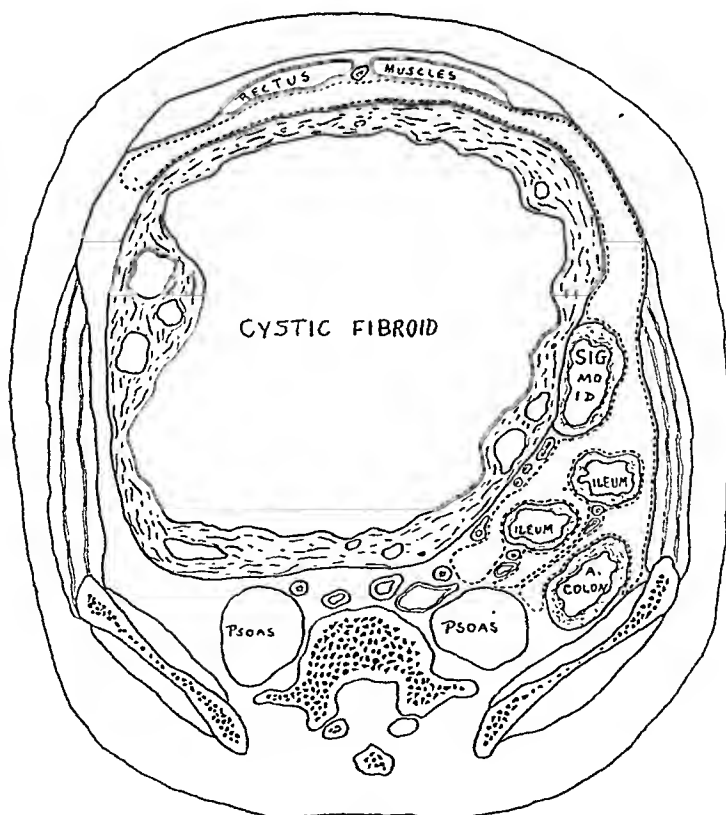


Fig. 3.—Diagrammatic cross-section through the abdomen above the level of the promontory. Peritoneum in dotted lines.

by a pedicle, three-fourths of an inch thick, from just below and behind the left uterine horn. It had developed between the layers of the left broad ligament, separating them widely, and had then stripped up the peritoneum from the entire left and posterior walls of the pelvis and abdomen to well above the pelvic brim. The left tube and round ligament coursed downward and around the lower pole. As the tumor extended further, it insinuated itself between the layers of the mesosigmoid and raised them and the parietal peritoneum from the posterior and left abdominal wall, so that the left layer of the mesosigmoid passed forward over the tumor and was reflected from it to the left abdominal wall in the anterior axillary line (Fig. 3). The sigmoid and its blood vessels lay in the wall of the tumor well over to the right side, and the right layer of the mesosigmoid passed from the tumor to the posterior abdominal wall considerably to the right of the midline. There was no plane of cleavage between the bowel and the tumor.

A long incision was made in the peritoneal covering of the tumor about one and one-half inches in front of the sigmoid, and by sharp and blunt dissection the bowel and its blood vessels were freed. There was profuse bleeding and many vessels had to be clamped and cut. The possibility of damage to the blood supply of the sigmoid was considered, but as the intestine showed no change in color by the end of the operation, we felt reassured. The tumor was then peeled off from the posterior and lateral walls of the pelvis and abdomen, dividing the peritoneal reflections as they were encountered. This left a large raw area on the posterior and left lateral pelvic and abdominal walls where the left ureter and the bifurcation of the aorta and iliac vessels could be seen plainly. A one-inch incision was made in the posterior vaginal wall, and two pieces of iodoform gauze were pushed through into the vagina to drain this raw area and the parametrial regions. Peritonization was easily accomplished, as there was much redundant peritoneum and the sigmoid could be swung back into its normal position where it covered much of the raw area. The abdominal wound was closed in layers with a small strip of rubber dam drain down to the aponeurosis through the lower angle of the wound.

At the conclusion of the operation the patient was moderately shocked but rallied quickly after a 500 c.c. transfusion, given immediately after her return to bed. Next day the hemoglobin registered 55 per cent, a drop of 25 per cent notwithstanding the transfusion. Her subsequent recovery was uneventful, she was out of bed on the fourteenth day and discharged on the seventeenth day. About a month later, she had a moderately severe attack of cholecystitis and several milder attacks since, which subsided under medical treatment.

When last seen, on Dec. 14, 1935, the patient was perfectly well, the wound was firmly healed, the cervical stump was freely movable, and there was no tenderness in the pelvis. Her weight was 244 pounds. The abdomen was markedly pendulous, and she is obliged to wear a specially fitted supporting corset.

CALCULATION OF THE WEIGHT OF THE TUMOR

Fluid drained off by trocar	3½ gallons	448 fluid ounces
Fluid retained in cyst	3 quarts	96 fluid ounces
Fluid spilled (approx.)	1½ pints	24 fluid ounces
Fluid in small cysts	1 pint	16 fluid ounces

Total quantity of fluid	584 fluid ounces
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584 fluid ounces = 641 ounces avoirdupois

Specific gravity of the fluid = 1.024

Correction for specific gravity, $641 \times 1.024 =$	656 ounces =	41.0 pounds
Weight of the empty shell		8.5 pounds

Total weight of the tumor	49.5 pounds
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135 CENTRAL PARK WEST

ABDOMINAL PREGNANCY AT TERM WITH DELIVERY OF A NORMAL LIVING CHILD

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IN THEIR comprehensive review of the literature of abdominal pregnancy, Cornell and Lash* (1933) report that in 86 cases in which the baby was born after the sixth month of gestation, the infant mortality was 22 per cent, whereas in the 60 cases in which the baby was born alive in the eighth and ninth months of pregnancy, it was about 35 per cent. Therefore, we feel that the presentation of another such unusual case is timely, more especially since the aforementioned authors report that deformities were quite common, many babies having more than one type. The maternal mortality was 14.3 per cent (34 cases) in the 236 cases gleaned from the literature, their private cases and the records of the Cook County Hospital. Peritonitis and shock accounted for 25 of the 34 deaths. We concur with the authors in believing that the mortality can be lowered greatly if we desist from interfering with the placenta. Packing with or without marsupialization will give the best results. Although hemorrhage may occur and prove fatal, as the placenta separates or disintegrates, it is far safer to leave the placenta alone, as this accident is rare.

In the reported cases, only 35 per cent were diagnosed correctly before operation and in this case the great distention interfered with an accurate examination. The presence of a mass in the lower abdomen which appeared like a distended bladder, and which did not disappear after catheterization should have assisted us in making a diagnosis, and finding the uterus separate from the fetus. The cervix was high, patent (because it had been previously dilated), and made one feel that labor had not progressed, because something was interfering with engagement, as well as causing intestinal obstruction.

M. L. F., 66814, negro female, aged nineteen years, admitted to the University Hospital from a rural district at 4:00 P.M. Jan. 8, 1935, with temperature 99, pulse 140, and respiration 26.

Primigravida apparently near term, gave history of having had abdominal pains for past eighty hours, which were thought to be labor pains. Engagement had not ensued, no progress had been made even with administration of castor oil, and attempted insertion of catheter. Mild distention with symptoms of intestinal obstruction was found. A history of a tedious pregnancy, fraught with ill health, excessive nausea and vomiting, continuous right-sided pain and umbilical pain (which at no time was "knifelike"), with frequent slight vaginal bleeding, was elicited.

Admission Examination.—Patient restless with a "fruity odor" to breath. Blood pressure 110/70, cardiac rhythm regular, pulse thready, hemic murmur present. Many fetal parts palpable, especially in lower abdomen, giving impression of transverse position, fetal movement felt, and fetal heart sounds elicited. Abdomen dis-

*Cornell, Edward L., and Lash, A. F.: Internat. Abst. Surg. (Supplement to Surg. Gynec. Obst.) 57: 98, 1933.

tended, especially in the epigastrium, very tender throughout, with prominence in the lower abdomen simulating a distended bladder which did not disappear after catheterization. Rectal examination showed a cervix with one-finger dilatation, but no effacement. Urinalysis showed marked acetonnuria, otherwise negative. White blood count 9,900. Red blood count 2,810,000, Hb. 50 per cent (Sahli). (Polymorphonuclears, 92 per cent; lymphocytes, 8 per cent; blood chlorides, 258 mg. per cent; nonprotein nitrogen, 42 mg. per cent; blood culture, negative.

Patient was given intravenous glucose and normal saline, subcutaneously, as supportive treatment during the night, and a high colonic irrigation returned clear. Morphine and other sedatives were administered. Vomiting continued during the night but was relieved by morning when the acidosis was reduced.

Preoperative Course.—At 10:00 A.M. (Jan. 9, 1935) vaginal examination revealed a firm cervix which would not retain a catheter, so a small pack was introduced. Outline of the fundus could not be determined because of abdominal distention. Surgical consultation agreed that a Porro cesarean section was necessary.

Operative Record.—The patient was considered a very poor risk, and operation was ordered to save the baby. Preoperative diagnosis: intestinal obstruction, possible peritonitis, pregnancy. A long midline incision revealed the abdominal wall to be very thin. The fetus was found free in the abdominal cavity, the sac having been ruptured. The peritoneal fluid was turbid. There was evidence of a generalized peritonitis. The intestines were greatly distended and there were masses of fibrinopurulent exudate on the intestinal walls. The baby was quickly delivered, slightly cyanotic but alive. The placenta was apparently over the large bowel and pelvic organs (later shown to be attached only to the uterus and the region of the right tube). The uterus was about the size of a twelve weeks' pregnancy. The cord was tied, and a marsupialization of the placenta was performed. Simultaneously in the upper left quadrant of the abdomen a jejunostomy was performed. A large wet dressing was placed over the placenta, and a smaller dressing placed over the upper incision. The patient left the operating table with very little change in her condition as gas oxygen anesthesia had been used.

Postoperative Course.—Patient was returned to the room and a Levine tube inserted through the nose to allow for gastric decompression. Fifteen hundred cubic centimeters of normal saline was administered and within two hours 500 c.c. of citrated blood was given. Patient was placed immediately under an oxygen tent, and for the first part of the night appeared to be holding her own. The overwhelming toxemia was apparently the cause of death fourteen hours after operation.

The fetus was well formed and weighed five pounds and two ounces. It left the hospital at the end of six weeks, weighing seven pounds and five ounces. There were no anomalies and development was perfect. There is no way of estimating the length of time that the fetus had been free in the abdominal cavity, although from the exudate and history, one would suppose that the onset of labor four days previous to operation had caused a rupture of the sac with the subsequent escape of the fetus into the abdominal cavity.

*Necropsy Findings.**—Projecting from a surgical incision in the lower mid-abdomen, there was a putrefying saclike structure forming a globular mass 10 cm. in diameter, from which protruded an umbilical cord. The peritoneal cavity contained some 500 c.c. of turbid, blood-stained, thick fluid, and everywhere the peritoneal surfaces were dull and the coils of intestine were lightly bound by sheets and flakes of fibrinopurulent exudate. The projecting sac, attached at its upper part by dense fibrous adhesions to the omentum, was a full-term gestational sac with a placenta 18 cm. in diameter, and was bound by fibrous adhesions to the sigmoid colon and seemed

*Necropsy report by Dr. Edgar R. Pund, Professor of Pathology.

to extend into the broad ligament on the right side, so that the right ovary in its own ligament lay behind the sac. Coming off from the sac laterally and posteriorly was the right tube which lost itself in the wall of the sac. Other than congestion there was nothing unusual about the left tube and ovary.

The cervix was soft and dilated, and the uterus measured 11 cm. by 7 cm. The endometrial surface was congested, cloudy, and shaggy. The right cornu was considerably stretched and the musculature of the uterus at the cornu lost itself in the gestation sac. The placenta was not detached and was apparently fixed to the structures of the right broad ligament, including the tube and the wall of the cornu of the uterus.

Microscopic examination of the gestational sac revealed a hollow viscus containing hypertrophied smooth muscle; the pregnancy therefore lay in the mural part of the isthmus of the tube. Suppurative inflammation of the uterine endometrium and of the gestational sac was found.

DIABETES COMPLICATING PREGNANCY

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DIABETES complicating pregnancy since the advent of insulin has very materially changed the outlook for mother and baby to such an extent that adding my experiences with two severe diabetic individuals would seem not to be remiss.

CASE 1.—Mrs. B., aged twenty-seven, para ii, gr. 0, first consulted me on June 15, 1934. Last period March 16, 1934. Diabetes was first recognized in October, 1931. She was immediately hospitalized, blood sugar 222 mg.; she was given a diet of protein 68, fats 101, carbohydrates 122, calories 1,669; weight was 104½ pounds; 30 units of insulin per day. She left the hospital after a week, went home, and immediately became pregnant and was aborted. She was constantly watched from then on. Weight came up to normal, 115 to 120 pounds, and frequent blood sugars read from normal to 175 mg. In December, 1933, she went into coma; blood sugar was 404 mg. From then on, until she became pregnant, she received from 40 to 60 units of insulin per day, frequently showing slight shock and at times drowsiness. She had the usual childhood diseases; her appendix and tonsils had been removed. There is no history of diabetes in the family. Examination showed a normal female type pelvis of good measurements; head, heart, lungs, and abdomen normal; a very healthy looking girl weighing 140 pounds. She had a very uneventful pregnancy, her blood pressure was always normal, and she showed no albumin in her urine. At five months she went into severe insulin shock, requiring intravenous glucose. Her diet, during her whole pregnancy, was kept constant. Her insulin requirements, during the first trimester, were about 40 units a day; during the second trimester, about 30 units; and during the third, about 50 units per day. Her basal metabolism rate was plus 5. Two weeks before term, due to a large baby, labor was started. Her weight was 159 pounds, blood pressure 120/60, urine, no albumin nor sugar. Quinine and castor oil were given, followed by a hot enema and six three-minute doses of pituitrin at twenty-minute intervals. This did not start labor, so her membranes were ruptured. Labor started immediately. The urine was examined every hour for sugar, diacetic acid and acetone, and was always negative. During her whole labor of ten hours, she was on the verge of insulin shock, requiring the juice of two dozen oranges. And, although she ate her normal supper during this time, only seven units of insulin were given. Her blood sugar, just before supper, after four hours in labor, was but 79 mg. When she was fully dilated, a male child weighing 8 pounds 5 ounces was delivered

by low forceps, L.O.A. The puerperium was entirely normal, blood sugar six hours after labor was 383 mg., and insulin requirements about 40 units per day. The baby had to be put in a respirator to start breathing. The baby did very well, was back to birth weight in twelve days. Repeated urine tests of the baby showed no sugar. This patient is now, six months after birth of baby, still taking 40 units of insulin.

CASE 2.—Mrs. E., aged twenty years, was first seen by me on Nov. 16, 1934. Her last period was Sept. 7, 1934. She has had diabetes for the past ten years. At first her blood sugar was 265 mg., with 17.5 per cent sugar in her urine, and 2-plus acetone. On a low calorie (800) and low carbohydrate (62) diet, which was used in those days, 24 units of insulin kept her sugar free. All during her childhood she had taken large doses of insulin, sometimes as high as 75 and 80 units a day. Her blood sugar has gone as high as 440 mg., and frequently over 300 mg.

Her grandfather died of diabetes at the age of seventy years and no other member of a large family has it. Her past history was negative except for childhood diseases. Physical examination showed nothing abnormal, blood pressure 110/60, weight 130 pounds, blood sugar 348 mg.; she is taking 54 units of insulin per day. Just before her pregnancy she was taking between 48 and 55 units per day. Her basal metabolism rate was plus 7. During her pregnancy her diet was kept constant and insulin requirements stayed the same. At five months she went into diabetic coma; 140 units of insulin in twelve hours, plus intravenous sugar, etc., brought relief. Thirty-three weeks after her last menstruation she weighed 139½ pounds. Blood pressure 120/60. Baby was small and breech presenting. She suddenly went into labor and one and one-half hours after first pain, and with only twenty minutes in the hospital, almost precipitated a sireniform monster. This lived for one hour. Immediately after labor her blood sugar was 142 mg., urine negative. She had a very uneventful puerperium; stayed on same diet and used same amount of insulin, which she is still doing.

I would also like to report a case of pseudodiabetes which cleared up immediately after insulin was stopped. Mrs. C., aged twenty-nine years, para i, gr. 0, menstruated last Nov. 20, 1933. She first consulted me on June 18, 1934, with a history of having sugar in her urine for the past three months. For some reason a blood sugar was not taken, but she was given gradually increasing doses of insulin until she was taking 30 units per day and was on a restricted carbohydrate diet. She showed 3-plus sugar in her urine. She had lost ten pounds during the last two weeks, was quite drowsy and reacted poorly to mental stimuli. She was immediately referred for a diabetic check-up; showed a blood sugar of 83 mg. After a few days of heavy carbohydrate diet her blood sugar was 85 mg., after, of course, stopping her insulin. There was some glucose, but mainly lactose in her urine. Later, sugar practically disappeared from her urine and she went to term, delivering uneventfully. Postpartum she showed no sugar in her urine and had a normal blood sugar on a regular diet. According to Bowcock and Greene, glycosuria does not carry with it a potential diabetic tendency. This case seems to illustrate this because on repeated urinary examinations, since her delivery, she has shown no sugar.

SUMMARY

1. Two severe cases of diabetes were carried through pregnancy and delivered normally.
2. Diabetes, like so many other medical complications in obstetrics, must be carefully treated and the pregnancy will take care of itself.
3. These two cases show that hypoglycemia is more to be feared than coma.
4. A severe case of renal glycosuria, unfortunately treated with insulin, is also reported.

A NEW AND EFFICIENT METHOD OF INFANT CIRCUMCISION

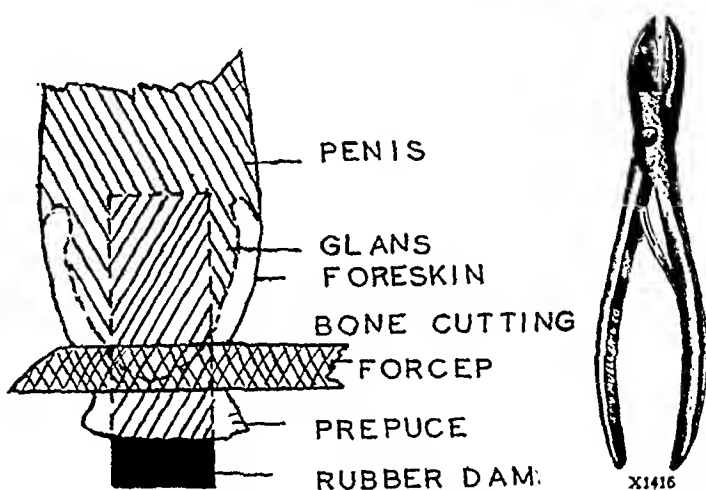
D. A. CALHOUN, M.D., TROY, N. Y.

O PINIONS vary as to the advisability of doing a circumcision on newborn babies. The operation is not indicated if the foreskin can be easily and thoroughly retracted, but subsequent operation is very often necessary because the retraction and cleansing is neglected by the mother after the infant goes home. It is, therefore, safe to say that under the prevailing conditions circumcision should be done before the baby leaves the hospital; subsequent attention is then unnecessary.

The ideal circumcision is one that can be done in the shortest time, with a minimum of trauma and pain; without sutures, and an absolute hemostasis. These qualifications together with a good end-result constitute an ideal surgical procedure.

Let me present the technic for such an operation which can be done any day before the infant goes home, one which not only fulfills all the above requirements, but can also be completed in about four minutes.

Preceded by proper personal surgical cleanliness, the penis is thoroughly cleansed with green soap and water. The tip of the foreskin is grasped laterally by small



mosquito forceps and enough traction is made to allow a thorough breaking up of the adhesions under the prepuce with any blunt instrument. Care that the adhesions are thoroughly broken up is essential, and adds to the success of the operation. Holding the two forceps in the left hand and exerting traction on the foreskin, a strip of rubber dam is inserted underneath and carried to the corona of the glans and left in situ. The rubber is three-fourths of an inch wide and two inches long. The thumb and forefinger can then easily force back the glans and identify the location of its tip. The bone forceps with its V-shaped surface toward the baby is applied just distal to the glans and closed tightly for three minutes. There is a momentary pain experienced by the baby at this point, but it lasts only a few seconds. After three minutes the superfluous tissue is severed with a sharp scalpel just distal to the instrument. After the forceps is removed the cut edge end of the rubber dam is seen to have separated the compressed tissues and the glans is exposed to view. Withdrawal of the remaining rubber causes the foreskin to retract upward and over the glans with its mucous membrane and skin edges sealed together throughout its circumference. No hemorrhage is present.

The after-care consists of a sterile dry dressing, and the parts should be kept as dry as possible until healing is complete. This usually requires only a few days.

DECIDUA POLYPOSA WITH ABNORMAL ADHESIONS*

JULIUS LEBOVITZ, M.D., WOODSIDE, N. Y.

THE decidual mucous membrane of the pregnant uterus may be the seat of many of the diseases that attack the endometrium of the nonpregnant uterus, with the exception that in the pregnant uterus the lesions and the histologic changes are modified incident to pregnancy. They often manifest themselves, however, in an exaggerated form due to the enormous hyperplasia of the decidual endometrium, which is an exaggeration of hyperplasia which occurs normally in the early months of pregnancy, in which the decidua instead of becoming thinner, as is normally the case, increases to considerable proportions. Another form of endometrial decidua change is the polypoid hyperplasia of the decidua. The decidua may show polyplike excrescences or projections of the entire hyperplastic endometrium or of limited areas.

Virehow was first to describe this condition in 1861, which he called decidua tuberosa and he considered it syphilitic in origin. In other cases, however, no cause whatsoever could be discovered, but probably there is a preexisting chronic endometrial affection that would account for it.

Schroeder also described this condition and observed that it usually ended in a miscarriage at the second or fourth month. Occasionally the pregnancy may be carried to term. Sometimes in abortion or labor the thickened decidua may cause abnormalities in the separation of the placenta and, incidentally, profuse hemorrhages.

Nyulasy compiled about 100 cases. He believed that syphilis is an etiologic factor and also noticed disturbances in the separation of the placenta. Bulius holds, however, that it occurs very rarely, and Williams stated that he has never seen such a case in his practice.

To illustrate the abnormalities in the separation of the placenta and the result of the profuse bleeding, I desire to present this case.

Patient, aged thirty-five years, family history negative. She had had the usual childhood diseases. Moderate habits. She started to menstruate when twelve years old, and after menstruation was established, it recurred at twenty-eight-day intervals lasting from three to five days. No history of any disturbance at any time. She has one child seven years old which was delivered instrumentally after a rather difficult labor. The postpartum convalescence was prolonged. She stayed in the hospital eighteen days after delivery. No conception for seven years. She was seen about the middle of February. The last menstruation was on Nov. 16, 1933. Upon bimanual examination, about a three months' pregnancy was found. On the twentieth of March, the patient gave a history of intermittent bleeding for the last five days, during which time she passed clots. On bimanual examination I found that the cervix was $2\frac{1}{2}$ fingers open, and the uterus was about the size of a four months' pregnancy. Temperature 98.6° , pulse 84, no abdominal tenderness, moderate bleeding from the cervix. Patient was removed to the Midtown Hospital, where a curettage was performed under $N_2O + O_2$ anesthesia. The removed placenta was beet colored. The vagina was packed with iodoform gauze. The patient stayed in the hospital

*Read before the Section on Obstetrics and Gynecology of the Medical Society of the County of Queens, April 19, 1935.

about four days; she had no temperature and made an uneventful recovery. She was discharged on the twenty-fourth of March. There was slight oozing for the first two days, after which it stopped. The pathologic report of the specimen is as follows:

Microscopic section showed among the clots, bits of decidual cell as well as numerous chorionic villi.

Patient was well after this. About two months later her menstruation returned. The menstruation was very profuse and lasted about ten days. The next menstruation began about three weeks later and lasted about sixteen days. On bimanual examination the uterus was found in ante flexion, and was of normal size somewhat hardened. I advised a diagnostic curettage which the patient declined. The following menstruation became more prolonged lasting from sixteen to twenty days, with short intermenstrual intervals, and there were just a few days when patient was free from any bleeding. Finally patient consented to a diagnostic curettage, and on the eighteenth of August, 1934, she was again admitted to the Midtown Hospital. On curetting, in the right corner of the uterus I found a somewhat hardened mass about the size of a hazelnut; it was intimately adherent to the uterine wall, which upon curetting bled profusely. The vagina was packed with iodoform gauze. The pathologic report of the curetting was as follows:

Tissue consisted largely of placental tissue which underwent necrosis, and there were a few portions of endometrium with normal cells and rich stroma which were infiltrated by lymphoid cells. There was no evidence of malignant change of endometrium or placenta.

After curetting, the patient stopped bleeding for the next four days. On the twenty-fourth of August the patient started to hemorrhage. This raised the question of the diagnosis. My impression was that in spite of the negative pathologic report of this curetting, there was still the possibility of the existence of a chorion-epithelioma or an intramural fibroid on top of which a partial adherent placenta could be present. In view of the excessive hemorrhage I decided upon hysterectomy. By this time the patient's hemoglobin was down to 45 per cent and the red blood cells down to two million.

On August 24, I gave the patient a transfusion of 800 c.c. of blood. The next morning I performed a supravaginal hysterectomy, under spinal anesthesia. Upon opening the abdomen I found the uterus in normal position somewhat enlarged and hardened; other pelvic organs were negative. When I opened the specimen I found a polypoid cystic mass in the right corner of the uterus about the size of a hazelnut firmly attached to the uterine wall. The pathologic report about this specimen was as follows:

Gross.—Uterus measured 6 by 5 by 3 cm. In the right cornu was a polypoid mass measuring 1 by 5.1 cm. attached to the mucosa and sharply delimited. It did not appear to invade the wall, although in one portion there was a fibrous core extending upward into the mass. On section, cut surface showed numerous large hemorrhagic cysts.

Microscopic.—The polypoid mass consisted of organizing chorionic villi firmly attached to the uterine walls, but not infiltrated. The blood spaces were tremendously dilated and contained early clots. This region was sharply delimited from the adjacent endometrium. At the edge the endometrium had very markedly dilated glands, but this changed very rapidly to the normal endometrium found over the remainder of the uterine cavity. The uterine wall had a moderately diffuse fibrosis. The serosal surface was normal. There was no evidence of malignancy either in the placental remains or in the endometrium.

Patient made an uneventful recovery and stayed in the hospital about ten days and is at present feeling well.

This case is interesting from the point of view that all possible abnormalities that a decidua polyposa could present were present in this case, such as interruption of pregnancy, abnormal adherency of the placenta, and profuse hemorrhages.

49-20 FORTY-THIRD AVENUE

MYXOFIBROSARCOMA OF THE OVARY*

C. H. HIXSON, M.D., WASHINGTON, D. C.

THE patient (Columbia Hospital, Case 70629) was a white female, aged twenty-nine years, had been married but now separated. She came into the hospital complaining of enlargement of the abdomen and gave the following history. On April 26, 1934, she noticed a hard, tender lump in her abdomen. A short time later, she began to have pains in her back. Her abdomen continued to enlarge and the mass had reached the umbilicus when she entered the hospital on Aug. 7, 1934. She did not have any symptoms of pregnancy except an amenorrhea. Her last menstrual period was about April 7 and the period previous was about a year ago. Her menstruation began when she was ten years old, with an interval of from twenty-one to twenty-eight days, and a duration of seven days. Until about a year ago her periods were regular. She had one pregnancy seven years ago, which was normal. There has been frequency of urination for the past two years. There was no history of previous operations or serious illnesses.

Physicalexamination revealed a fairly well-nourished female with a normal temperature, pulse, and respiration. General physical examination was essentially negative. The abdomen contained a large, firm, tender and slightly movable mass extending to the umbilicus which, on vaginal examination was found nearly filling the pelvis. It was diagnosed as a leiomyoma of the uterus. She was operated upon on the ninth of August and found to have a large tumor of the right ovary, adherent to the uterus, which was pushed backward and to the left. The adhesions were separated easily, and the tumor was dissected from its peritoneal covering and removed together with the tube.

The pathologic report was:

Gross Examination.—The specimen was a large, relatively soft ovarian tumor, measuring 17 by 16 by 10 cm. in its greatest dimensions. The sectioned surfaces were very moist, glistening, and soft with multiple cystic cavities filled with clear fluid.

Microscopic Examination.—The tumor was composed of very small spindle- and stellate-shaped cells with small, dense, irregularly shaped nuclei and fairly evenly distributed nuclear chromatin. The cytoplasmic boundaries were indistinct, and there was a considerable amount of loose fibrillar intercellular stroma. In some areas the myxomatous appearance was more prominent than in others. Mitoses were relatively infrequent.

Diagnosis.—Myxofibrosarcoma.

Although the histologic appearance of this tumor was that of a fibrosarcoma with myxomatous degeneration, the clinical course should be favorable unless adhesions were present. If the tumor was adherent to the surrounding structures local recurrence may be expected.

*Presented at a meeting of the Washington Gynecological Society, November 23, 1935.

The postoperative course was febrile, the temperature reaching 104° about two weeks after operation. She was very weak and a blood transfusion was given. The febrile curve gradually receded and her strength gradually increased. She was discharged on Sept. 5, 1934, and referred to Garfield Hospital for x-ray treatment. She received treatments from Sept. 22 to Oct. 11, 1934, over anterior and posterior portals of pelvis, duration eleven minutes, 200 roentgen units, 200 kilovolts at 50 cm.

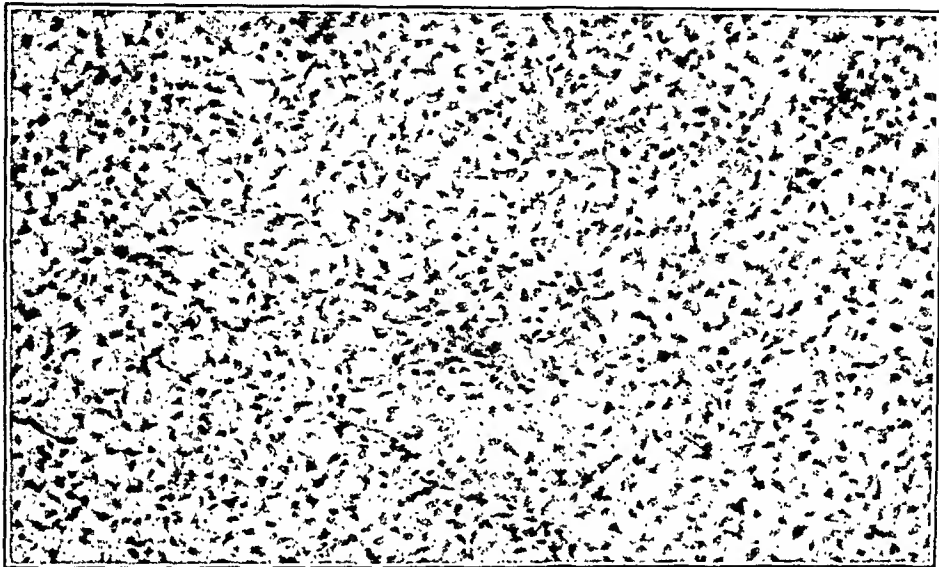


Fig. 1.

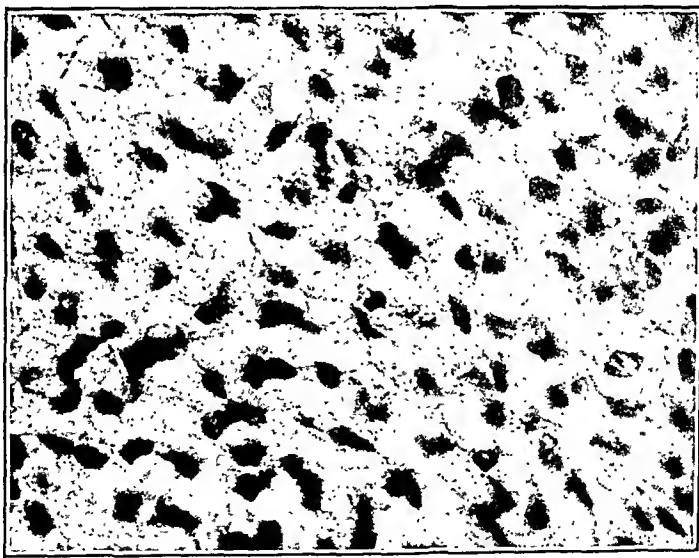


Fig. 2.

distance. She received twenty of these treatments over an area of 20 cm. square, to the blistering stage. At the beginning of the treatment, an Aschheim-Zondek test was positive.

On the twelfth of July, 1935, she returned to the hospital x-ray department and was feeling perfectly well. Her weight was 109 pounds, a gain of eleven pounds. Vaginal examination at this time revealed a movable, cervix, soft, broad ligament remnants clear, no induration in either side. There were no palpable masses, and no palpable enlargement of inguinal or other lymph nodes.

ABDOMINAL ANEURYSM*

FREDERICK H. FALLS, M.D., CHICAGO, ILL.

THIS report deals with a colored female, twenty-seven years of age, who came into the Cook County Hospital on the twentieth of November, saying she had been sick for two months, and complaining of pain on both sides of the lower abdomen shooting into the groins. The examining room diagnosis was pelvic abscess. The temperature was 100° when she entered the ward. It then went up to 102° and 103°, and she appeared toxie. On abdominal examination there was a tumor mass on the left side, and on pelvic examination the lower pole of this mass could be felt in the pelvis on the left side. The mass was expansile and pulsating. The diagnosis made was abdominal aneurysm. She was transferred to the medical ward with that diagnosis, and there an x-ray plate was made which confirmed the diagnosis. The aneurysm broke and the patient died seventeen days after entering the hospital. Before she died there was a progressive paresthesia and anesthesia of the lower limbs, and pain had been felt in the lower left limb. Blood count showed 2,400,000 red cells, 55 per cent hemoglobin, and 22,000 white cells, which gave rise to, and supported, the diagnosis of pelvic abscess. The differential count showed 86 per cent polymorphonuclears, 10 per cent lymphocytes, and 4 per cent monocytes.

Autopsy.—The abdominal cavity contained about 600 c.c. of partially coagulated blood. Distal to the descending colon and sigmoid, and extending to the midline, there was a large mass which was covered by peritoneum. It extended into the pelvis, displacing the lowermost portion of the sigmoid and colon to the right. The lower one-third of the abdominal aorta contained up to 50 c.c. of clotted blood. In the left lateral wall there was a defect 13 by 8 mm. The walls formed a huge sac measuring 32 cm. in length, 13 cm. in breadth, and 11 cm. anteroposteriorly. The posterior wall of the sac was formed by the psoas muscle which was infiltrated by dark brown blood clots.

Aneurysms of the abdominal aorta are relatively rare. At Cook County Hospital there have been 16 aneurysms of the abdominal aorta, occurring in both men and women in the last nine years. The total number in women were four or 25 per cent, three colored and one Mexican. In the males there were four white patients and eight colored. Of the four cases that occurred in women, three were aneurysms extending into the pelvis. In one case the iliopsoas muscle formed the posterior aneurysmal sac. In another case the aneurysm extended into both common iliacs, and in a third it extended into the bifurcation of the aorta.

30 NORTH MICHIGAN AVENUE

*Read before the Chicago Gynecological Society, December 20, 1935.

METASTATIC CARCINOMA TO THE OVARY FROM THE VOCAL CORD*

J. D. KIRSHBAUM, M.S., M.D., CHICAGO, ILL.

(From the Department of Surgical Pathology of the Cook County Hospital)

IN A review of the literature and the autoptic records of the Cook County Hospital since 1929, no report was found of metastasis to the ovary from the larynx. This case is unique in that the patient was only twenty years of age when a carcinoma of the right vocal cord was detected, and approximately one and a half years later metastasis occurred to the left ovary.

H. L., aged twenty, an unmarried white female, first entered the Cook County Hospital, April 5, 1934, complaining of hoarseness for four months. She had no other complaints and did not appear acutely ill.

Examination of the throat revealed an ulcerated, irregular, infiltrating lesion of the right vocal cord and ventricular band. A biopsy was taken and revealed a basal cell carcinoma. The remaining examination was essentially negative. The blood Wassermann was negative.

Under avertin anesthesia, the right vocal cord and ventricular band were removed up to the vocal process and the base of the lesion was diathermized. A permanent tracheotomy was performed. Twelve hundred milligram hours of radium was applied to the outside of the neck. Eleven days later the patient was discharged from the hospital. She returned to the hospital Sept. 30, 1935, approximately eighteen months later, complaining of a mass in the abdomen. She stated that she felt well following her tracheotomy until four months ago when she first noticed the mass in her abdomen which had been progressively growing larger. Her menstrual periods had become more frequent and prolonged, lasting eleven days with an interval of seven days between periods. The menstrual flow is blackish to brownish in color, stringy in character and contains blood clots. Her appetite had been poor, she felt weak and had lost some weight.

Examination revealed a firm smooth tumor mass extending for four fingers above the umbilicus, movable, extending more to the left of the midline and not attached to the abdominal wall. The tumor mass felt cystic and could be moved to the left easily.

Pelvic examination revealed the uterus to be of normal size and position and freely movable. The adnexa were difficult to palpate because of the tumor mass.

The heart and lungs were essentially normal.

The diagnosis was made of an ovarian cyst, but metastasis to the abdomen had to be considered. An x-ray picture of the chest was negative for metastasis.

The patient refused a local anesthesia and ether had to be resorted to, since gas could not be given through the tracheotomy tube.

Operation was performed by Dr. H. Jackson on the fourth of October through a midline incision. A few cubic centimeters of clear yellow fluid were seen in the abdominal cavity, and a disklike mass 12 by 8 by 6 inches was found growing from the left ovary. The mass was solid and felt rather soft in places. The right ovary appeared of normal size and unchanged. The patient made a subsequent uneventful recovery.

*Read at a meeting of the Chicago Gynecological Society, December 20, 1935.

On the fifteenth of October some small cervical lymph nodes on the right side of the neck were felt and she was, therefore, transferred for radium therapy. Ten radon seeds were inserted into the mass of the neck. On the thirtieth of October the patient menstruated for three days. She was seen this week and although she has been receiving deep x-ray therapy to the abdomen, she has developed nodules in the right breast, although the glands in the neck have disappeared.

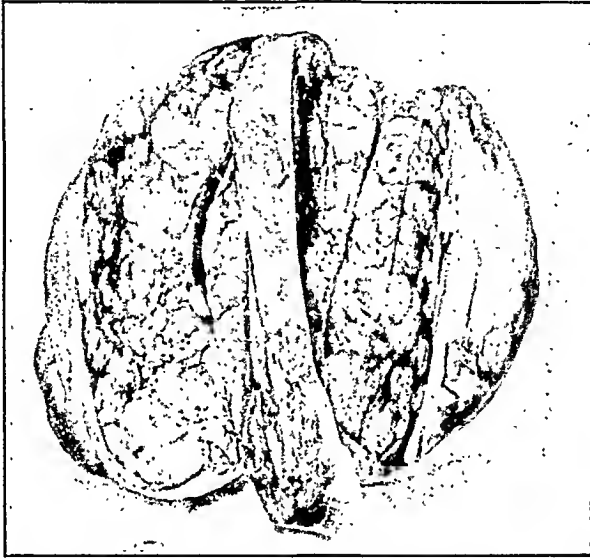


Fig. 1.—Photograph of ovary substituted by tumor tissue.

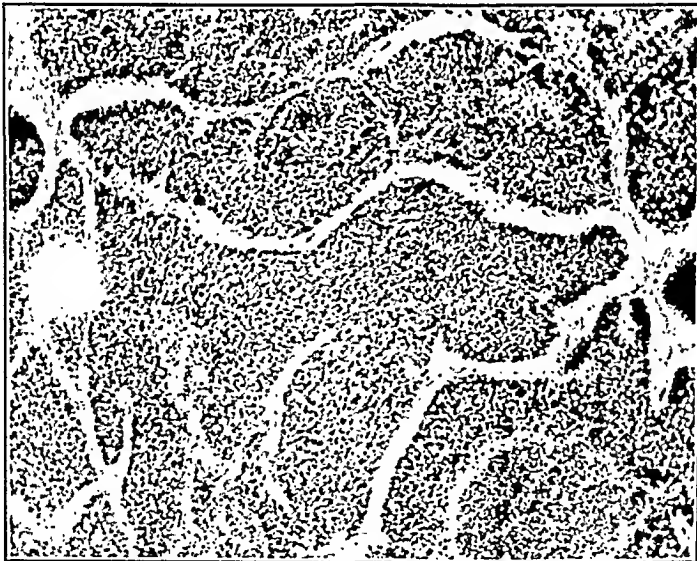


Fig. 2.—Microphotograph showing basal cell carcinoma of the ovary.

Pathologic Examination.—Specimen was an ovary converted into a solid tumor mass 20 by 17.5 by 7.5 cm., about the size of a large grapefruit. The surface was smooth purple gray and was encapsulated. Adherent to the surface was a thin-walled patent fallopian tube. In this region the mass fused with an elevated lobular mass, about the size of a hen's egg and corresponded with the original site of the ovary. On sectioning the mass was found to be solid pale purple tan and appeared lobulated. In the center there was a cavity 9 by 4 cm. in diameter and filled with recent blood. It was lined by smooth purple gray membrane.

Microscopic examination from various sites revealed a uniform picture. The tumor was composed of solid alveoli of small cells with hyperchromatic oval to round nuclei. The alveoli in places were centrally necrotic and were separated by thick bands of connective tissue. There were numerous mitotic figures noted.

The histologic picture of the tumor of the right vocal cord showed a similar picture, a basal cell carcinoma.

Diagnosis: metastatic carcinoma of the left ovary, basal cell in type, from the right vocal cord.

Patient died subsequently and at autopsy metastatic deposits were found in the brain but not in any other organs.

INTERSTITIAL PREGNANCY*

A. E. KANTER, M.D., CHICAGO, ILL.

MRS. R. G., twenty-five years of age, was admitted on the Gynecologic Service at Mount Sinai Hospital on Dec. 18, 1935 with a tentative diagnosis of ectopic pregnancy. Her complaints were backache of two years' duration, headaches and dizziness for one month, and a menstrual irregularity.

Her last regular menstrual period was on Sept. 11, 1935. She had no period in October. On about November 10 the patient began to bleed from the vagina, the bleeding being profuse accompanied by the passage of clots and lower abdominal cramps. This bleeding lasted for about two weeks. Following this the patient was free of signs of blood for five days after which she again bled, but only a very slight amount for five days. Since then there has been no bleeding but the patient has not felt well, having an aggravation of the backache, headaches and dizziness, and having noted a steady loss of weight.

The past medical and surgical histories were of no particular significance. The patient had had two full-term normal pregnancies five and two years ago. Previous menstrual history was normal, the patient menstruating every twenty-eight days, the period lasting three to four days with no dysmenorrhea. She had been having some frequency of urination and some loose stools in recent months.

The laboratory investigation revealed a white blood count of 6,250 with a 68 per cent polymorphonuclear leucocytic count in the differential. Red blood count was 4,410,000. Hemoglobin 75 per cent. The urine had a positive albumin test.

Bimanual palpation revealed a multiparous introitus with a moderate relaxation of the anterior and posterior vaginal walls. The cervix was soft and presented a granular erosion of both anterior and posterior lips. The corpus uteri was in third degree retroversion, somewhat enlarged, and softened. In the right adnexal region, attached to the right uterine horn, was a mass the size of a small orange which was firm and not tender. The left adnexal region was negative.

On December 20 exploratory posterior colpotomy was done. When the right horn of the uterus was delivered through the posterior culdesac a semicystic purplish red mass, the size of a goose egg, was found to occupy the entire cornu of the uterus and to be continuous with the isthmus of the right fallopian tube. This mass was the interstitial pregnancy on the right side. By the vaginal route the right horn of the uterus was resected with the cornual mass in situ. The wall of the uterus was closed with two layers of catgut and peritonization was accomplished by the use of the severed tube and its peritoneum. Curettage revealed a very small amount of endometrium. The posterior peritoneum and mucosa were closed by interrupted sutures of chromic catgut.

*Read before the Chicago Gynecological Society, December 20, 1935.

American Journal of Obstetrics and Gynecology

EDITORS: GEORGE W. KOSMAK, M.D., AND HUGO EHRENFEST, M.D.

Editorial Comment

Carcinogenic and Estrogenic Substances

CANCER research has been greatly extended in many directions since the purification and chemical identification of some of the carcinogenic substances. The discovery that many of the carcinogenic substances likewise have estrogenic properties has resulted in much experimental work and speculation. The possibility of a deleterious effect following the administration of estrogenic substances has been broached by the Council on Pharmacy and Chemistry.*

As pointed out in a recent editorial in the *Journal of the American Medical Association*,† the pioneer experiments of Lathrop and Leo Loeb‡ showed that removal of the ovaries reduces the incidence of mammary cancer, while those of other investigators showed that stimulation of the breasts by estrogenic hormone favored the growth of experimental tumors. To draw definite or final conclusions from such type of experiment and to apply them to the human being appears entirely unwarranted, as unwarranted as to consider as cancer the changes noted in the repeatedly traumatized cervix of experimental animals stimulated with this type of hormone.§

Under the local stimulating effect of the sex hormones, the vascularity and lymph supply of breast and pelvic organs is greatly increased. That transplanted cancer tissue, therefore, will show an increase of takes and a more rapid growth in these sites is readily understandable. Yet it is a far cry from this observation to evaluate this as specific tumor stimulation. Transplanted breast cancer likewise, as long as the cells retain any of the physiologic characters of mammary tissue, will also respond to any of the hormonal mammary stimuli irrespective of their new location.

The observations of many clinicians, long before these experimental questions were broached, showed that the rapid growth of breast

*Report; J. A. M. A. 100:1331, 1933.

†Editorial; J. A. M. A. 106:1093, 1936.

‡Lathrop, A. E. C., and Loeb, L.: J. Cancer Research 1:1, 1916.

§Overholser, M.D., and Allen, E.: Proc. Soc. Exper. Biol. & Med. 30:1322, 1933.

cancer in pregnancy could be modified by termination of pregnancy and removal of the ovaries. The monthly stimulation of the mammary gland in the human being must to some degree account for the frequent occurrence of breast carcinoma in the female, as compared with that of the male. The frequency of adenocarcinoma of the uterus might perhaps be ascribed, at least in part, to the monthly stimulation which the womb undergoes, and nature provides a partial safeguard against this danger by the cyclical desquamation of the endometrium. Therefore, imperfect menstruation without desquamation and the continued chronic hyperplasia of the mucosa might favor adenocarcinoma. Howard Taylor, Jr., in his statistical paper,* finds some evidence favoring such an hypothesis. On the other hand, although the cervix undergoes a minimal amount of cyclical change, carcinoma of this subdivision of the womb is frequent. Here, however, the long-continued irritation, due to chronic inflammations, must be considered as an important additional factor.

Considerable evidence therefore obtains that on the one hand extraneous substances of the phenanthrene group and related structure have a distinct carcinogenic action. The evidence of estrogenic properties shown by some of these carcinogenic substances is of extremest theoretical interest. More than this cannot be positively claimed at this time.

If one desires to enter the realm of pure speculation, it is stimulating to realize that the nucleus of both the male and female sex hormones, and cholesterol are closely related. Cholesterol circulates in the blood at all ages. It is fascinating to theorize upon the possibility that the liver may synthesize not only the sex hormones, for an estrogenic reaction may be obtained with the urine of human female castrates,†, but also intermediate products which might prove to be carcinogenic. These metabolites may offer a new opening for the study of the ever present question of cancer genesis. In the interim, however, the conflicting findings so far accumulated should not be used to hamper the clinical employment of estrogenic substances until more evidence, as to possible dangers arising from their use, has been accumulated. As yet no convincing contraindications have been discovered, unless the two mice treated by Lacassagne from infancy on with estrogenic and prepituitary substances which then developed the one thymic cancer, the other uterine malignancy (?), be so considered.‡

—Robert T. Frank.

*Taylor, H. C., Jr.: AM. J. OBST. & GYNEC. 23:309, 1932.

†Frank, R. T., Goldberger, M. A., and Salmon, U. J.: Proc. Soc. Exper. Biol. & Med. 33:615, 1936.

‡Lacassagne, A.: Compt. rend. Soc. de biol. 121: 607, 1936.

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

INVESTIGATION AND ANALYSIS OF PUERPERAL DEATHS IN MEMPHIS

JAMES R. REINBERGER, M.D., MEMPHIS, TENN.

(From the Department of Obstetrics, the University of Tennessee)

IT IS generally conceded by those studying maternal mortality rates that the negligible difference in gathering mortality figures does not account for the persistently high maternal mortality prevailing in the United States. This fact was recently substantiated in Dr. Elizabeth Tandy's report, "Comparability of Maternal Mortality Rates in the United States and Certain Foreign Countries."

The burden of this sad commentary should not fall entirely upon the physician's shoulders as is generally accepted. In 1923, this analysis was begun, about the time that Memphis was accepted into the National Birth Registration area, when 90 per cent of the births were registered, which is the lowest prerequisite for admission.

Memphis has been an ideal city for study. Both our City and County Health Organizations have cooperated to the fullest degree; and without their aid, this survey could not have been made. The initial step in the survey was made to ascertain the true facts relative to the care of all patients. This reveals the true obstetric transition.

This twelve-year study indicates that a progressive, evolutionary, obstetric process is well under way. There has not been a tremendous increase of births. Only 4,217 were recorded in 1923; the intermediate peak, 5,157 for 1930; with a decided decline, 4,821 for 1934. This apparent early increase in births, at least for this section, may be largely attributed to increased birth registration.

In viewing the tremendous increase in hospitalization of both white and colored patients, one can see the desire for better obstetric attention. A steady increase is noted even in the number of colored patients delivered by white and colored physicians. This is evidence of the greater desire for not only better facilities for delivery, but also for better professional service. The midwife has been practically eradicated, for in 1923, 524 patients were delivered by them in contrast to 49 in 1934. This radical change in attitude could not have been accomplished unless a substitute had been offered to those unable to pay for better medical attention. The solution of the problem at hand was education of the public to realize the necessity of good attention and to provide means of applying knowledge thus gained. Memphis overcame these obstacles. This was magnificently accomplished through a most unique service, jointly rendered by the physicians of the University of Tennessee, who provided the educational program, and by the nurses of our local Board of Health and City Hospital, who supplied the facilities for both home and hospital deliveries.

This very decided, progressive change failed to show the expected lowering in our maternal death rate. The mortality has varied only a fraction of 1 per cent

per thousand live births since this study was begun. It is obvious then that more information of the individual deaths is necessary before the present mortality rate can be accepted.

In an attempt to clarify the reason for this consistent high mortality, all cases admitted to our University Clinic, with deliveries throughout the city, were compared; and a tremendous difference in their death rate was found. Our clinic cares for about 50 per cent of all deliveries in Memphis.

This comparison showed the value of prenatal care, for during the past eight years the death rate has been from six to fifteen times greater in patients not having prenatal supervision. This has almost eliminated death from toxemia. Deaths from hemorrhage and dystocia were reduced. But, unfortunately and particularly in the negro race, there still remain too many deaths from puerperal infection. It is hoped that a more intensive prenatal examination relative to distant foci of infection with more treatment for genital infection during pregnancy will reduce the incidence of puerperal infection in the future. The general acceptance that mortality rates are twice as great in the negro as in the white has failed to be a contributory factor in our mortality; because the deaths are divided into 82 for the whites, in contrast to 72 for the colored. The lack of prenatal supervision has, however, accounted for many unnecessary deaths.

The records of all hospital deaths and all home deaths since 1923 were analyzed. This more detailed study was not only necessary, but was prompted by lay and medical articles inferring that increased hospitalization was not only contributory to, but was responsible for, this sustained mortality.

The number of nonresident deaths was astonishing.

A geographic study for nonresident deaths covered a radius of 150 miles; the majority were within 50 miles. This area included portions of Arkansas, Mississippi, and Tennessee. It was responsible for 83 or 53.1 per cent of all deaths, which were divided into 27 for 1932, 25 for 1933, and 32 for 1934. It is significant that the deaths were fairly constant in number and localized in this three-year study. Thus far it has not been feasible to survey the local problems of all rural deaths, but a more detailed analysis was made in Shelby County. This county was responsible for only 2 deaths in 1932, 5 in 1933, and 7 in 1934; or, a total of 14.1 per cent of all rural deaths. It was again evident that the deaths were fairly well localized. During this three-year period of investigation, there were 2,853 births with 14 deaths or 4.8 per cent. This is three times as great as deaths of the city. This survey shows that over 50 per cent of all patients are still being delivered by midwives and almost 95 per cent were negroes. It is therefore clear why the death rate has remained high. It must be largely for economic reasons, because over 60 per cent of all patients delivered in 1934 were registered for some sort of prenatal supervision. The Shelby County Health Department recognized this unfortunate condition, and last year established seven prenatal centers in the offices of private physicians. These physicians serve without compensation even though most of these patients will ultimately be delivered by midwives. This is a distinct step forward. It is not illogical to believe that similar conditions prevail in other rural sections.

Analysis of the cause of death was also considered as a necessary factor in the solution of this problem.

Unfortunately this survey revealed nothing unusual. Sepsis and hemorrhage accounted for 36 or 23 per cent of all deaths from abortions; but sepsis accounted for 57 or 36 per cent of all deaths. Toxemias of pregnancy, for 42 or 26 per cent; hemorrhage, for 18 or 11.5 per cent; dystocia, for 15 or 9.6 per cent; medical complications, for 14 or 9 per cent; ectopic pregnancy, for 8 or 5.1 per cent; and undetermined, for 2 or 1.3 per cent. As usual there have been too many deaths from sepsis, toxemia, and hemorrhage. Medical deaths could have been prevented by prenatal medical examination; dystocia resulted in too many deaths, but was

under the usual proportion of those dying from other preventable causes. In most instances the deaths from ectopic pregnancy were attributed to the patients who failed to consult physicians early enough, rather than the failure of diagnosis, for most of the patients were moribund upon admission to hospital. Of course, the two remaining undetermined sudden deaths could not be explained.

During the years of 1932, 1933, and 1934, 13,688 births were recorded with 156 deaths or 1.14 per cent. It is not only suggestive, but significant, that 71 per cent of all deaths occurred in charity patients with only 29 per cent attended by private physicians. It is also important to note that even the individual hospital having the smallest number of nonresident deaths has the lowest mortality. The causes of death as reported on the death certificate were compared with the actual description of the cases by the physicians. Many times the records were of no value or so vague that conclusions had to be drawn from only brief physical findings, internes' and nurses' notes. For study the 156 deaths were divided into four groups: (1) Patients admitted for abortion and ectopic pregnancies, 35 or 23 per cent; (2) patients delivered in hospitals, 84 or 54 per cent; (3) patients admitted postpartum, 27 or 17 per cent; (4) home deliveries, 9 or 6 per cent.

Abortion and ectopic pregnancies accounted for 36 or 23 per cent of all hospital deaths which were principally due to hemorrhage and sepsis. This group of cases comprised an almost unbelievable number, and will in the future assume a more alarming proportion due to the increasing incidence of criminal abortion. No one can estimate the exact number of criminal abortions performed in Memphis. It cannot be coincidental that so few resident deaths resulted, while most of the deaths from abortion were recorded in nonresident patients. In an effort to substantiate this reckoning, a survey was made of all abortions treated in the Memphis General Hospital for the year of 1933. From 201 patients treated, 35 per cent admitted criminal abortion. These cases were analyzed with reference to the type of treatment and end-results. There were only 2 deaths in this series. They died within twenty-four hours after admission.

We believe that this small percentage of deaths was due to the method of treatment. All patients were treated by elevation of bed, noninterference, and uterine stimulants. Instrumentation was performed in only 7 per cent of all cases of which only 2 required dilatation and curettage for repeated hemorrhage; the remaining of these were treated by a simple sponge stick removal. It is only fair to conclude from this comparative study that the method of treatment and the circumstances under which this was rendered are the pertinent questions, but the failure of the patient to seek medical attention cannot be ignored, for many sought attention too late.

Full-term deliveries accounted for 84 or 54 per cent of the total number of deaths in hospitals, while 9 or 6 per cent occurred in the home, which actually leaves 111 cases of full-term hospital deaths. Twenty-seven or 17 per cent of the patients who died were admitted to the hospital following delivery for complications, principally hemorrhage and sepsis. Since these patients who died postpartum were not associated with hospitalization, they will be dismissed, as most were sent in too late for effective therapy.

The 84 patients or 54 per cent of the 111 cases to be analyzed more closely were delivered in hospitals. Forty-eight or 36 per cent of the patients who died had received no prenatal supervision and died within the first twenty-four hours. Fourteen or 1.5 per cent of the patients who died delivered in hospitals were assigned to medical and undetermined causes. This leaves only 22 deaths or 15 per cent that could have been associated with improper medical attention or hospitalization. It is evident from the records that many of these patients who died within the first twenty-four hours could not have been saved. However, it is felt that, had a more thorough physical examination been made or better obstetric judgment been ex-

exercised, some could have been saved. Too many patients were immediately operated upon for eclampsia, while the operation was delayed too long in others. Some deaths from hemorrhage and exhaustion of labor from dystocia could have been prevented if the usual methods of resuscitation had been applied before delivery.

Medical attention can be held responsible only for this remaining 22 or 15 per cent of deaths. Education, economy and lack of cooperation of patients are responsible for the remaining 134 or 85 per cent of all deaths. The actual corrected mortality for these 22 deaths in 11,688 hospital births is 0.19 per cent in contrast to the accepted mortality of 1.14 per cent. It should not be overlooked that 9 deaths occurred in 1,827 home deliveries or 0.50 per cent. This reveals one death for every 538 hospital births in contrast to one death in every 203 home deliveries. Therefore, home deliveries are 2.6 times greater than hospital deliveries. This study concludes that increased hospitalization with all its so-called contributory factors, analgesia and instrumentation in perfectly supervised cases, has not helped to sustain the present accepted high maternal mortality.

The following conclusions presented in this survey clarify this maternal welfare problem. This survey shows that:

1. The maternal mortality rate of 1.14 per cent is too high.
2. The present accepted mortality rate is obtained only from data on the death certificates and does not reveal the true status.
3. Hospitalization has not increased, but has actually lowered, the mortality.
4. The value of hospitalization for all acutely ill patients has been accepted by the laymen and physicians. This accounts for the large number of deaths.
5. Increased hospitalization has served as a means of studying large groups of deaths whose true status could not have been otherwise determined.
6. Abortions are responsible for 36 or 33 per cent of all hospital deaths and increase the statistical maternal mortality.
7. Full-term deliveries in hospitals accounted for 34 or 54 per cent of all deaths, while 9 or 6 per cent occurred in the home.
8. Twenty-seven or 17 per cent of all deaths were sent into the hospital for complications following delivery.
9. Forty-eight or 36 per cent of all hospital deliveries had received no prenatal attention and died within twenty-four hours; 14 or 9.5 per cent died from medical or undetermined causes.
10. Twenty-two deaths or 15 per cent should be considered as a medical correctable factor in the sustained mortality rate.
11. Nonresident deaths contributed 83 or 53.1 per cent of the mortality.
12. The economic contributory factor is not coincidental, for 71 per cent of all deaths occurred in charity patients.
13. Rural sections have not interested themselves sufficiently in this problem, or have been unable to provide funds for correction.
14. Education, economic status and lack of cooperation of patients are responsible for the remaining 134 or 85 per cent of all deaths.
15. In general, physicians and State and County Medical Societies have recognized their obligations to this problem. They are appointing maternal welfare committees to awaken keener interest.
16. Cooperation from federal and civic organizations will be necessary in order to obtain funds for the solution of this maternal welfare problem.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

Meeting of January 14, 1936

The following papers were presented:

Polyneuritis of Pregnancy. Dr. Arthur W. Bingham. (For original article see page 144.)

Motion Picture of the Anatomy and Technic of the Parametrial Fixation Operation. Dr. Robert T. Frank.

Dr. Frank stated that for a period of over twenty-five years he had sought for a satisfactory operation for the cure of uterine prolapse and the one about to be described was the best method he had found.

"Some years ago I checked up on 414 patients who had been treated by the method which was employed at Mount Sinai for many years, namely, anterior and posterior colporrhaphy with ventral fixation. Dr. Max D. Mayer and Dr. Howard E. Lindeman studied these cases and found that only 66 per cent of the cases gave satisfactory results, and of the unsatisfactory ones 21 had ventral hernias. That was extremely discouraging, particularly as the most seriously ill patients were operated upon by the men on the service who had had the most experience. It appeared that the results varied inversely to the experience of the operator, the worse the case the worse the result, the more often the hernia. Then I tried vaginal hysterectomy, not very many cases, doing a fairly elaborate operation, such as was advocated by Dr. G. G. Ward, Dr. Goff, the Mayos, etc. Before I discarded the operation, except in cases where for some reason a prolapse was present and the uterus had to be removed as well, as for fundal carcinoma, I found that simple vaginal hysterectomy with adequate resection of the vaginal walls gave as good a result as the more elaborate techniques. Then I thought that perhaps the operation which was so commonly used in England and which according to their follow-up, and I will say that their follow-ups were extremely lax from our point of view, very often depending on post-card data, was so marvelously successful that I saw no reason why it should not be tried. Then I essayed to find somebody who knew the operation, but was unable to find any one. So I went ahead myself from the descriptions which I could find, which were mainly those of Fothergill and Shaw, and while I saw much suturing I found little anatomy. Therefore, I had to work it out, step by step, until I understood both the anatomy and the operation.

"I claim no originality whatsoever. The operation was first done by Donald of Manchester in 1888. Fothergill and Shaw were his pupils and continued it. Donald was not the type of surgeon given to writing, so Fothergill and Shaw did the describing and popularizing of the operation. Therefore, if you wish to attach the name of any man to the operation it should be known as Donald's or perhaps the Manchester operation.

"Halban described the operation through one of his pupils, Meentids, in 1932, who called it Halban's operation, although he had only done it from 1919 on, and I will add in passing that he understood the anatomy of the operation fully.

"Recently, Professor Tandler said to me: 'The operation is based on entirely false principles, but clinically it is successful.' I am unwilling to concede this because Tandler's point of view is that the musculature of the pelvis, particularly the levators, is the structure which supports the uterus. I think all who are familiar with

vaginal hysterectomy, where there is no prolapse, will agree that as soon as the broad ligaments are cut, the uterus will descend with ease, and I personally think that it is the broad ligaments—I do not mean the intraperitoneal thin portion, but the bases of the broad ligaments—which normally hold the uterus, the levators taking up the extra shocks as a shock absorber.

“The operation is based on the following:

“That the amputation of the cervix with exposure of the broad ligaments is followed by an aseptic condensation of these elastic tissues, the same type of condensation that you find after an inflammatory process, say, a frozen pelvis: these tissues never returning to their previous resiliency. The operation can be used for any case in which, under an anesthesia, the portio can readily be pulled down to the introitus. It can be used too in the most extreme cases of prolapse, and, furthermore, it can be used in those difficult cases where a prolapse of the cervix develops after a supravaginal hysterectomy.”

CHICAGO GYNECOLOGICAL SOCIETY

Meeting of December 20, 1935.

The following paper and case reports were presented:

A study of Three Hundred and Eight Cases of Placenta Previa. Dr. F. C. Irving (by invitation). (For original article see page 36.)

Abdominal Aneurysm. Dr. F. H. Falls. (For original article see page 164.)

Interstitial Pregnancy. Dr. A. E. Kanter. (For original article see page 167.)

Metastatic Carcinoma to the Ovary from the Vocal Cord. Dr. J. D. Kirshbaum. (For original article see page 165.)

A Case of Carcinoma-Sarcoma of the Uterus. Dr. Carey Culbertson.

BROOKLYN GYNECOLOGICAL SOCIETY

Meeting of November 1, 1935

Report of a Case of Cyclops. Dr. David Kupferstein.

Meeting of December 6, 1935.

The Effects of Progestin on Afterpains. Dr. Samuel Lubin and F. J. Clarke. (For original article see page 134.)

Results of Treatment in Placenta Previa. Dr. Joshua Ronsheim. (For original article see page 139.)

Total Hysterectomy by the Abdominal Versus the Vaginal Route in Benign Uterine Disease. Dr. E. H. Richardson, Baltimore, Md. (by invitation). (To be included in the October issue.)

WASHINGTON GYNECOLOGICAL SOCIETY

Meeting of November 23, 1935

The following papers were presented:

Further Improvement in Pelvimetric Roentgenography. Dr. J. Bay Jacobs. (For original article see page 76.)

Myxofibrosarcoma of the Ovary. Dr. Clayton H. Hixson. (For original article see page 162.)

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Myoma

Witherspoon, J. Thornwell: Possible Cause of Uterine Fibroids, *Endocrinology* 17: 703, 1933.

That hyperplasia of the endometrium is the result of follicular hormone stimulation, unopposed by any corpus luteum influence, and with a possible anterior pituitary lobe association in the background has been definitely proved. Since the uterus as a whole is involved in the reproductive process, the action of estrin should not be limited solely to the endometrium; the myometrium should also be involved, and all the more so when the estrin stimulation is abnormal. It is this fact that the author wishes to present as a possible cause of uterine fibroids. The endometrium is in a constant state of change, and it is easy to see that any abnormal stimulation to the uterus should first be manifested in the endometrium. The growth of fibroids is not noticeably rapid, and consequently any stimulation to the myometrium which causes fibroids would have to persist over a rather lengthy period. The assumption is advanced that the unopposed action of estrin on the uterus results first in immediate endometrial changes, characterized by hyperplasia, and secondly in more latent myometrial disease in the nature of fibroid growths.

Using the above hypothesis as a basis, the cases of 26 subjects of hyperplasia of the endometrium, operated on and diagnosed as such, and on whom a second operation for multiple fibroids was performed after an approximate interval of four years and four months, are analyzed. In addition, 124 cases of fibromyomas in white women and 125 in colored women, diagnosed microscopically, are offered with the associated ovarian and endometrial findings, as presenting added evidence in support of a cause and effect relationship between hyperestrin stimulation, hyperplasia of the endometrium, and fibromyomatous growths of the myometrium.

J. THORNWELL WITHERSPOON.

Clason, S.: Uterine Myomas in Young Women Under Twenty Years of Age, *Acta obst. et gynec. Scandnav.* 15: 29, 1935.

Clason reports a case of a girl of sixteen who had a large myoma of the uterus. This is the youngest patient operated upon and reported in the literature. From a review of the literature the author comes to the conclusion that the frequency of myomas in women under twenty years of age is less than 1 in 1,000. He believes that a pyemic constitution predisposes to myomas.

J. P. GREENHILL.

Randazzo, M.: Sterility and Uterine Fibroids, *Monatsch. f. Geburtsh. u. Gynäk.* 98: 270, 1935.

The relationship between uterine fibroids and sterility is a double one. There is no doubt that uterine fibroids can cause sterility. On the other hand, there is no unity of opinion among gynecologists that sterility may be the cause of the development of myomas. We know that fibroids frequently occur in elderly, unmarried women and in nuns, i. e., among women whose reproductive functions are not exercised. The author attempts to solve the connection between sterility and the development of myomas. He first shows that the ovaries stimulate the growth of the fibroids. From a study of 358 cases of fibroids he tries to show that the sterility which is associated with fibroids is due only in small part to the presence of the myomas. He found that in 60 per cent of the cases the interval of time which elapsed between the last pregnancy and the discovery of the fibroids was more than six years. He feels justified, therefore, in assuming that the sterility was not only the possible but the actual cause of the growth of the fibroids. He adds that there must be, of course, a predisposition to the development of the tumors. The sterile or slightly fertile woman develops a fibroid as if a biologic law of woman punishes her because she either wilfully or involuntarily does not propagate.

J. P. GREENHILL.

V. Jaschke, R.: Circulatory Apparatus and Myomata, *Arch. f. Gynäk.* 155: 6, 1933.

In 962 patients with fibroids, 601 (62 per cent) had an absolutely normal circulatory apparatus. Only 77 patients (8 per cent) showed cardiac changes which might be related to the presence of the tumors. The remainder had arrhythmias, functional murmurs, valvular disease, thyroid hearts, etc. In 21 of the 77, the heart muscle damage could be attributed to emphysema, malnutrition, previous infectious diseases, etc. The remaining 56 women showed definite myocarditis and the effects of prolonged secondary anemia. These cardiac changes must be attributed to the protracted bleeding and the severe secondary anemia rather than to the presence of the myomas since the same type of changes are found following the hemorrhages of carcinoma, metropathia hemorrhagica and in all other forms of severe secondary anemia. The term "myomaheart" is a misnomer. Myomas per se have no effect upon the heart or the circulatory apparatus.

RALPH A. REIS.

Cotte, G., and Mathieu, J.: Some Cases of Spontaneous Phlebitis During the Evolution of Uterine Myomas, *Gynéc. et obst.* 30: 209, 1934.

In the opinion of Cotte and Mathieu, the appearance of phlebitis during the evolution of a myoma should always be considered as a serious complication, since, in addition to accidents which may arise from the phlebitis itself, it may be followed by an infarct or an embolus. In cases where there are no complications it is not necessary to interfere. However, where it is urgent to operate, as for example in a case of an infected myoma with gangrene, one may ligate the hypogastric veins before removing the tumor. This necessity is rare. After spontaneous cure of phlebitis it is unwise to wait for a spontaneous cure of the myoma. It is best to remove the tumor by myomectomy or hysterectomy. By these procedures not only accidents due to the myomas but also the recurrence of phlebitis are prevented.

J. P. GREENHILL.

Ahlthrop, G.: Spontaneous Rupture of the Myoma Capsule, *Acta obst. et gynec. Scandinav.* 14: 368, 1934.

Ahlthrop collected from the literature 7 cases of spontaneous rupture of the capsule of a myoma and adds a case of his own. An analysis of the case reports indicates that the following factors are probably of importance in the origin of this rare complication: nutritional disturbances in the myoma associated with rapid growth of the tumor; pressure necrosis in the capsule; reduced elasticity of the capsular tissue; and retained contractile power of the uterus.

J. P. GREENHILL.

Harding, Warren G., and Hankins, Franklyn D.: Rhabdomyoma of the Uterus, *Arch. Path.* 16: 480, 1933.

A case of rhabdomyoma of the uterus is reported in a three-year-old child. The symptoms were foul-smelling and later bloody vaginal discharge, fever and anorexia. The important physical findings were: a sloughing tumor mass in the vagina and a secondary anemia. An exploratory laparotomy revealed an extra-peritoneal tumor in the anterior portion of the pelvis, the bulk lying between the bladder and uterus and extending into the broad ligaments. Postoperatively high voltage roentgen therapy was given and the immediate recovery was uneventful, except for the vaginal discharge. One month after operation an anuria developed, the abdomen became distended and the tumor enlarged. The patient died suddenly with evidence of pulmonary edema.

Postmortem Findings.—The growth rose to the level of the uterovesical fold, involved the trigone of the bladder and both ureters were compressed. The entire uterus was replaced by neoplastic tissue; no metastases were found. Microscopically, the growth consisted of well-differentiated tissue resembling adult striated muscle, and another portion composed of anaplastic tissue resembling fibrosarcoma. The number of mitotic figures was small; the round cells of the anaplastic tissue appeared to be typical myoblasts; and all stages of differentiated striated muscle could be found. The intimate association of anaplastic tissue with striated muscle cells in an area where voluntary muscle is not normally found suggests that both tissues are related histogenetically. The embryologic character of this voluntary muscle tissue is further indicated by the location of the nuclei in the center of the cell, by the clustering of the nuclei and by the presence of abundant intercellular connective tissue.

W. B. SERBIN.

Hamant, Chalnot, and Vichard: The Treatment of Large, Infected Polyps of the Uterus, *Bull. de la Soc. d'obst et de gynéc.* 23: 653, 1934.

The authors report two cases of large infected polyps of the uterus. One patient died and the other recovered after treatment. These polyps, which are in reality submucous, pedunculated fibroids, are characterized by their tendency to bleed, by their frequent spontaneous delivery, and by local or general infection which is usually extremely serious. The patients who are not operated upon as a rule die slowly of septicemia. The proper kind of operation to perform is not easy to decide upon. The following operations may be performed: (1) Vaginal removal of the polyp. This is the simplest of all operations but is serious because it is followed by a high mortality. The most recent statistics indicate a death rate of 60 per cent. The fatalities are due to hemorrhage which is difficult to control in an already anemic patient, injury to the uterine wall, and severe infection. (2) Vaginal hysterectomy. Rapid removal of the uterus through

the vagina with a minimum of shock removes at one time a large amount of toxins, and it assures drainage of the pelvic canal. This operation is frequently followed by vesicovaginal fistulas because of the friability of the tissues in the vagina. Infection following these operations is also frequent. (3) Abdominal hysterectomy. This operation permits complete hemostasis, protection of the abdomen and maximum drainage. The authors prefer subtotal hysterectomy.

J. P. GREENHILL.

Hamant, A.: Why Is It Necessary to Perform Myomectomies? *Bull. de la Soc. d'obst. et de gynéc.* 7: 631, 1933.

When, during the course of an operation, fibroids of the uterus are found, many surgeons perform an immediate hysterectomy. Hamant believes, however, that in many of these cases, a less radical operation should be done, namely, myomeetomy. He has thus far performed 156 such operations and all were followed by success except in one patient who died of a heart complication. The author considers myomectomy to be a simple, easy operation, not accompanied by any morbidity or particular mortality. This statement holds true not only for the simple cases but also for the complicated ones. In twenty of Hamant's cases, pregnancy followed the myomectomies. Some women had two, three, and even four pregnancies following the operation. Hence myomectomy is truly a conservative operation after which the obstetric history is entirely satisfactory.

J. P. GREENHILL.

Read, Charles D., and Bell, Arthur C.: Hysterectomy—Subtotal and Total, *J. Obst. & Gynec. Brit. Emp.* 40: 749, 1933.

The morbidity of 1,739 cases of subtotal hysterectomy was 20.6 per cent, and of 605 cases of total hysterectomy 27.1 per cent. The mortality of the subtotal operation was 2.1 per cent as compared with a mortality of 3.1 per cent for the total. The authors conclude: Each of the two operations considered has a definite place in gynecologic surgery. The sequelae following the subtotal operation are more numerous, and of more serious consequences than those following the total operation. Taking into consideration the remote deaths due to these sequelae, the remote mortality rate of the subtotal operation is considerably raised. The routine employment of total hysterectomy is not advocated, but the scope of the subtotal operation is distinctly limited. The fact that few women who have borne children have completely healthy cervixes should lead to the more general employment of the total operation. The subtotal operation still has a place: (a) In nulliparous women with healthy cervixes when hysterectomy is required for a benign condition; (b) in a few benign cases when the poor general condition of the patient contraindicates the more severe and prolonged operation; (c) in benign cases which fall into the hands of those who are inexperienced in gynecologic surgery. The total operation, for benign conditions, is indicated in all cases demanding hysterectomy in which the cervix is unhealthy and the condition of the patient does not contraindicate the operation.

WILLIAM F. MENGERT.

Guthmann, H., and Atzert, W.: Operation or Radiation Treatment of Myomas, *Monatsch. f. Geburtsh. u. Gynäk.* 98: 321, 1935.

A series of 501 cases of myoma was analyzed by the authors. In this group 245 were radiated, 185 were operated and 71 were not treated. The results of radiation and operation were almost identical. In the group of cases treated with

complete x-ray doses there was clinical healing in 93.6 per cent, and in the group which received a smaller amount of x-ray treatment a cure was accomplished in 85.9 per cent. For the patients who had a total extirpation of the uterus, complete recovery occurred in 93 per cent and for those who had enucleation of the fibroids, 82.4 per cent were cured. Among the operative cases there was a primary mortality of 4.8 per cent.

The complications subsequent to either treatment are: menopausal symptoms, increase in weight and difficulty during coitus.

The menopausal symptoms occur with equal frequency in the rayed and operated patients, namely, in 87 per cent. With one ovary preserved menopausal disturbances appeared in only 63 per cent of the cases. Even after enucleation alone, symptoms of the menopause appeared in 23.5 per cent. Hence, the psyche plays a very important rôle in menopausal symptoms.

Increase in weight appeared to be the same for both groups of cases. Abnormal increases in weight occurred in about 5 per cent of both series.

Difficulty during coitus as the result of involution of the vagina, occurred with the same frequency in the operative and radiated groups (13 to 14 per cent).

The author concludes that both radiation therapy and operation are useful in the treatment of myoma. The choice of therapy will depend upon the type of myoma, the complications, the age of the patient, the desire to retain menstruation and prevent nervous disturbances.

J. P. GREENHILL.

Goldenberg-Bayler, S.: *The State of Uterine Fibromas After the Menopause*, *Gynécologie* 34: 39, 1935.

After the menopause uterine fibroids may manifest themselves clinically even though they have remained quiescent for many years. In the majority of cases the reawakening of symptoms is due to degeneration of the fibroid or to associated uterine or adnexal lesions. When hemorrhage occurs in a case of uterine fibroids after the menopause, it is not necessarily a sign of malignancy. Likewise the absence of bleeding does not rule out a malignant growth. The other symptoms which are associated with fibroids after the menopause, namely, pain, leucorrhœa, and bladder symptoms, do not necessarily point to cancer. Among 322 fibroid patients treated in the author's clinic, 284 were found before the menopause, 25 during the change of life, and 11 after the menopause. The only efficient treatment for fibroids after the menopause consists of abdominal or vaginal hysterectomy because it permits radical extirpation of the fibroids and the associated lesions.

J. P. GREENHILL.

Pastiels: *A Case of Fibromyxoma of the Ovary*, *Bruxelles-méd.* 14: 1302, 1934.

The fibromas of the ovary, and above all the fibromyxomas, are rare tumors which clinically are only exceptionally diagnosed. They are usually taken for pedunculated uterine fibroids, or dermoid cysts of the ovary. A case of fibromyxoma of the ovary is reported in a woman twenty-nine years old. The menstrual periods began at fifteen years, and have been regular ever since. There is one child three years old. At operation a small amount of clear ascitic fluid was found. The right adnexa were easily accessible, but the ovary was totally transformed into a tumor mass of regular contour, but very hard. On section the tumor was resistant to the knife; it presented no cavities, and was finally diagnosed as fibromyxoma.

J. THORNWELL, WITHERSPOON.

Items

American Board of Obstetrics and Gynecology

The following were certified at this Board's Annual Meeting of May 11 and 12, 1936:

LIONEL BRAUN, Detroit, Mich.	RAYMOND D. MCBURNEY, Los Angeles, Calif.
PRESTON T. BROWN, Phoenix, Ariz.	WILLIAM B. MCGEE, San Diego, Calif.
THOMAS K. BROWN, St. Louis, Mo.	HAROLD K. MARSHALL, Glendale, Calif.
WILLIAM J. BULL, Montclair, N. J.	WILLIAM A. MICHAEL, Peoria, Ill.
LOUIS A. BUNIM, Brooklyn, N. Y.	GILBERT MONBACH, Cincinnati, Ohio
ARTHUR S. CALMAN, New York, N. Y.	HAROLD S. MORGAN, Lincoln, Neb.
F. BAYARD CARTER, Durham, N. C.	FRANK P. MURPHY, Omaha, Neb.
LEWIS E. DANIELS, Detroit, Mich.	WAVERLY R. PAYNE, Newport News, Va.
HAROLD B. DAVIDSON, New York, N. Y.	GEORGE F. PENDLETON, Kansas City, Mo.
JOSHUA W. DAVIES, New York, N. Y.	JEAN PAUL PRATT, Detroit, Mich.
NICHOLSON J. EASTMAN, Baltimore, Md.	NATHAN REIBSTEIN, Brooklyn, N. Y.
JOHN NORTON EWER, Oakland, Calif.	ARTHUR M. REICH, New York, N. Y.
MARSHALL FIELD, Chicago, Ill.	DONALD C. RICHARDS, Easton, Pa.
GLEN K. FOLGER, Cleveland, Ohio	WILLIAM GERALD ROGERS, Oklahoma City, Okla.
GEORGE H. GARDNER, Chicago, Ill.	SAMUEL A. RUBEN, Washington, Pa.
HENRY J. GOUBEAUD, JR., Brooklyn, N. Y.	RICHARD B. SCHUTZ, Kansas City, Mo.
MAURICE E. GRIER, Omaha, Neb.	JALMAR H. SIMONS, Minneapolis, Minn.
FRANKLIN E. HALL, Chicago, Ill.	THOMAS J. SIMS, JR., Kansas City, Kan.
HARRY E. HARVEY, Lincoln, Neb.	FRANKLIN D. SINCLAIR, Tulsa, Okla.
F. L. HEINEMEYER, Rockford, Ill.	DUDLEY R. SMITH, St. Louis, Mo.
GREY JONES, St. Louis, Mo.	SAMUEL B. SOLHAUG, Minneapolis, Minn.
F. A. S. KAUTZ, Cincinnati, Ohio	SIDNEY J. STONE, Cleveland, Ohio
WILLIAM T. KENNEDY, New York, N. Y.	JULIUS H. SURE, Milwaukee, Wis.
RAYMOND C. KING, Toledo, Ohio	HOWARD P. TAYLOR, Cleveland, Ohio
ARTHUR K. KOFF, Chicago, Ill.	MADLINE J. THORNTON, Madison, Wis.
FRED B. KYGER, Kansas City, Mo.	BENJAMIN E. URDAN, Milwaukee, Wis.
HERMAN H. LARDARO, New York, N. Y.	JOHN A. URNER, Minneapolis, Minn.
WILLIAM LEVINE, Brooklyn, N. Y.	ALBERT T. WALKER, Portsmouth, Va.
CLIFFORD B. LULL, Philadelphia, Pa.	JOSEPH B. WEISS, New York, N. Y.
	ANTHONY WOLLNER, New York, N. Y.

Of 91 applications for certification, during the year 1935 and 1936, 10 were either rejected or voluntarily withdrawn prior to examination; and of the 81 candidates examined, a total of 22 were failed or conditioned, and 59 were certified by the Board.

The next written examination and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology will be held in various cities in the United States and Canada on Saturday, November 7, 1936.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Bldg., Pittsburgh (6), Pennsylvania. Applications for this examination should be filed in the Secretary's Office sixty days prior to the scheduled date of examination.

American Gynecological Society

At the annual meeting of the American Gynecological Society, held at Absecon, N. J., May 25 to 27, the following officers were elected:

DR. FRED J. TAUSSIG, *President*

DR. GEORGE W. KOSMAK, *First Vice President*

DR. SIDNEY A. CHALFANT, *Second Vice President*

DR. RICHARD W. TELINDE, *Secretary*

DR. WILLIAM C. DANFORTH, *Treasurer*

DR. B. P. WATSON, DR. HILLIARD E. MILLER AND DR. NORMAN F. MILLER, *members of Council*.

Errata

In the article by Erwin von Graff, published in the May issue of the JOURNAL, page 758, Table I, Dr. D. A. Horner of Chicago is quoted as having published four cases with one recovery and three deaths. This is incorrect. There were only three cases and all recovered.

In the May, 1936, issue, page 796, there appears my discussion of a paper by Eugene Auer on "The Effects of Radiation on Cancer of the Cervix."

When my attention was called to it, I was chagrined to realize my carelessness in having approved for publication, this combination of inaccuracy and poor taste. The technic of radium therapy used by Max Cutler, Chief of the Tumor Clinic of the Michael Reese Hospital, is precisely the same as that used in the Curie Institute of Paris. This method has been used for many years and the end-results are well known and have been recorded in the literature on numerous occasions.

The average dose of radium applied in the vagina and cervical canal for the treatment of carcinoma of the cervix in the Tumor Clinic of the Michael Reese Hospital is 7,500 mg. hours and the maximum total dose is 8,000 mg. hours. The vaginal radiation is given over a period of 116 hours and the cervical radiation over a period of 70 hours. This is followed by external radiation either with the 4 gm. radium pack or with high voltage x-rays.

Concerning the end-results, Dr. Cutler, whose experience in the treatment of carcinoma is vastly greater than mine, is convinced that for carcinoma of the cervix, heavier doses spread over longer intervals and combined as above are the best available treatment.

I regret exceedingly both the technical errors and the unintentional unfavorable criticism in the published discussion.

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Chicago, Ill.

American Journal of Obstetrics and Gynecology

VOL. 32

AUGUST, 1936

No. 2

Original Communications

A STUDY OF FIBROMYOMAS OF THE UTERUS WITH RESPECT TO THE ENDOMETRIUM, MYOMETRIUM, SYMPTOMS, AND ASSOCIATED PATHOLOGY*

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AND CARL P. BAUER, M.D., F.A.C.S., CHICAGO, ILL.

*(From the Department of Obstetrics and Gynecology, Rush Medical College of the
University of Chicago.)*

IN ANY study of fibromyomas the primary consideration should be that of the etiology of these tumors. At the present time there are several theories which merit consideration. Robert Meyer¹ propounded the idea that the appearance of myomas represents a thickening of the already present muscle bundles which are directly connected with the normal uterine musculature. De Snoo² developed the contention that the origin of fibromyomas is in the undifferentiated cells which he termed the genitoblasts. Embryologically the uterus proper is derived from these cells, some of which remain dormant in their embryonic state to become active in providing the material for the growth of the uterus during pregnancy and for the regeneration of the endometrium during the puerperium. Under certain conditions abnormal stimuli transpose these latent genitoblasts into fibromyomas, adenomyomas, and endometriomas. A third hypothesis is based upon the conjecture that the walls of blood vessels provide the tissue from which fibromyomas are fashioned. Graves³ theorized that the production of these tumors is a process somewhere between true physiologic hypertrophy and actual neoplastic formation.

*Read before the Chicago Gynecological Society, January 17, 1936.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

Somewhere in the foregoing maze of evidence probably lies the answer to the etiology of the primary focus for the production of the fibroid tumors, but we must search further to find the factors that might be responsible for the stimulation of the "seed" fibroids to produce tumors of appreciable size. Pregnancy has long been considered an important element in the energizing process that brings size to fibromyomas because of the increase in thickness of the uterine muscle fibers and the markedly exaggerated blood supply to the pelvis that acts as a nourishing agent for incipient aberrant growths. By the same process of increasing blood supply, pelvic infections are deemed to be of importance as stimulators of tumor growth. More recently Witherspoon⁴⁻⁷ has stated that the most active of the exciting causes is the endocrine factor. By dint of much study and interpretation he has developed the hypothesis that hyperestrinism is the main, if not the sole, agent responsible for the growth of fibromyomas. His evidence makes much of the frequent occurrence of fibroid tumors in association with cystic oophoritis (microcystic disease of the ovary) and pelvic infection, conditions in which the circulating estrin reserves are greatly increased over the normal because of the failure of follicle rupture. If such an idea is correct, it would dovetail very nicely with the previously mentioned possible stimulating factors (pregnancy and pelvic infection), since in both instances there is, besides the increased blood supply, a great increase in estrogenic hormone content.

With the advent of the study of fibromyoma stimulation by estrin, Witherspoon made attempts to associate the production of such tumors with the appearance of hyperplasia of the endometrium, adenomyosis and endometriosis on a similar endocrine basis. In view of these factors we undertook this study in an attempt to aid in clarifying this situation and to make a correlation between these pathologic entities and the clinical histories in a series of cases. The present report embraces a group of unselected patients with uterine fibromomas, studies being made upon 100 women, 69 white and 31 colored.

GROSS PATHOLOGY

A résumé of the gross pathology present in this group of women will prove of interest and may be of value in our final analysis and summation. The size of the tumor present varied from that only slightly larger than normal to the proportion of a full-term pregnancy, the size being distributed as follows:

SIZE OF TUMOR	WHITE	COLORED
6 to 8 weeks' pregnancy	38	4
3 to 6 months' pregnancy	30	20
Over 6 months' pregnancy	1	7

Since salpingitis must be kept in mind as a possible factor in the supplying of estrin excesses, we must tabulate the numbers of patients in whom this type of pathology was present. This group includes all types of tubal involvement (chronically thickened and clubbed tubes, hydrosalpinx, pyosalpinx, hematosalpinx, pseudofollicular salpingitis, and tuboovarian abscess). Evidences of these types of inflammation were found in 3 of the white women and 26 of the colored. Cystic oophoritis was present in 8 of the colored women but in none of the white. Cystic oophoritis without salpingitis was found in 5 of the white women and in no colored woman.

Of the other pelvic pathologic conditions encountered in conjunction with the fibromyomas, laceration, erosion, and infection of the



Fig. 1.—Subbasal adenomyosis.

cervix was present 12 times, vaginal relaxations 7 times, external endometriosis 9 times, endometrial polypi 6 times, prolapse of the uterus 3 times, papillary cystadenoma of the ovary twice, and each of the following once: carcinoma of the body of the uterus, lymphogranuloma inguinale, acute appendicitis, dermoid cyst of the ovary, bartholinian cyst, and pregnancy.

MICROSCOPIC PATHOLOGY

At this point it is wise to define the terms we apply to the various microscopic pictures encountered in order that misunderstanding be avoided.

Adenomyosis.—An invasion of endometrial glandular structures into the myometrium.

Subbasal Adenomyosis.—The presence of glands from the basal layer lying deep in the uterine musculature (Fig. 1). These glands are always in the proliferating stage and do not take part in the menstruating function.

True Adenomyosis.—True adenomas containing all elements of the endometrium found in definitely circumscribed areas deep in the uterine wall (Fig. 2). These tumors menstruate parallel to the endometrium and may, therefore, be found in any stage in the menstrual cycle.

External Adenomyosis or Endometriosis.—True adenomas, such as described above, situated outside the uterine cavity or myometrium, e.g., chocolate cysts of the ovary, free upon the uterine serosa, on the external surfaces of the ovaries, tubes, bowel, or in the rectovaginal septum.



Fig. 2.—True adenomyosis.

Internal Adenomyosis was found to be present 44 times in the white women and 8 times in the colored. Of these, 30 white women and all 8 of the colored women had subbasal type of adenomyosis while 14 of the white patients displayed the true type. External adenomyosis (endometriosis) occurred 9 times among the white women and was entirely absent in the colored. Of this group 3 had chocolate cysts of 1 or the other ovary and the remaining 6 had the type that is distributed on the surface of the uterus, ovaries, etc.

The most striking feature of the study of the endometrium proper in these cases was the lack of uniformity in the thickness of the endometrium, all degrees and types of hyperplasia being found under varying conditions of associate pathology. Our criteria for hyperplasia of the endometrium are the same as those described by Cullen⁸

and Novak and Martzloff.⁹ Following this classification, we found 53 patients who demonstrated the presence of endometrial hyperplasia as follows:

TYPE OF HYPERPLASIA	WHITE	COLORED
Glandular	20	7
Interstitial	4	10
Swiss cheese	4	1
All combined	3	1
Polypoid	3	0

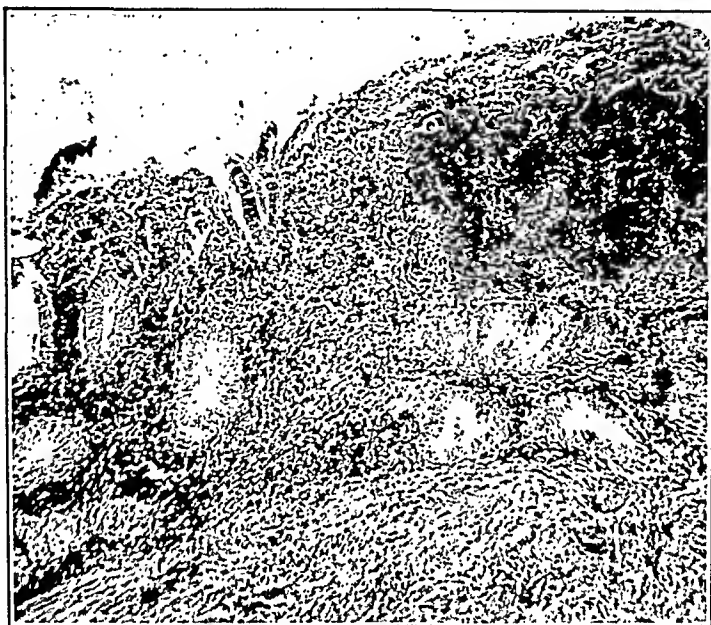


Fig. 3.—Dilatation of basal glands in menopausal endometrium.



Fig. 4.—Atrophy and hypertrophy of the endometrium.

Two distinct types of endometrial atrophy were noted during the course of this study, the true menopausal type with narrowed endometrium, few glands, and occasionally dilated glands in the basal layers (Fig. 3), and the atrophy seen in actively menstruating women with fibromyomas, the areas of endometrium lying directly over a

submucous tumor showing atrophic changes, while that in other places was normal or hyperplastic (Fig. 4). We found 24 of the women in this series displaying menopausal atrophy of the endometrium, 7 showing dilatation of the glands in the basal layer and 17 showing absence of such glandular dilatation. There were 3 patients in whom non-menopausal atrophy was evident.

True endometritis with round cell and plasma cell infiltration of the endometrial tissue was present in 3 of the colored patients. Edema of the endometrium was noted 29 times, 17 in the white and 12 in the colored patients. An interesting observation was that in some instances, although we were dealing with a proliferating stage endometrium, there existed a very definite capillary dilatation with infiltration of blood into the endometrial stroma. Such a situation prevailed 17 times in this group, 11 among the white patients and 6 in the colored.

For purposes of completeness, it was thought advisable to classify the patients in this series according to the stage in the menstrual cycle at which the endometrium was removed for study. The following table divides the women into their various groups:

Early proliferating stage	25
Late proliferating stage	9
Early secretory stage	23
Late secretory stage	31
Menopausal	12

A study of the fibromyomas themselves revealed that in 20 instances changes had taken place in their microscopic structure. Eleven showed hyaline degeneration, 6 early necrobiosis, 2 edema, 1 sarcoma, and 1 lymphangiectatic degeneration.

Since the cardinal symptoms of fibromyomas have for a long time been taught to be menorrhagia, dysmenorrhea, and leucorrhœa, it was felt that a correlation of these symptoms with the location of the tumors in the uterus and the presence of adenomyosis might prove of interest. The following tables express these correlations most adequately:

<i>Menorrhagia:</i>	WHITE	COLORED
Submucous fibroids	16	9
Submucous fibroids, adenomyosis	22	2
Subserous, intramural fibroids	3	2
Subserous and intramural fibroids and adenomyosis	6	1
<i>Dysmenorrhea:</i>		
Submucous fibroids	8	5
Submucous fibroids, adenomyosis	13	1
Subserous, intramural fibroids	3	2
Subserous and intramural fibroids and adenomyosis	5	5
<i>Leucorrhœa:</i>		
Submucous fibroids	8	4
Submucous fibroids, adenomyosis	6	0
Subserous, intramural fibroids	1	1
Subserous and intramural fibroids and adenomyosis	1	0

Twenty-one of the patients in this group had none of the cardinal symptoms of fibroids but had such miscellaneous complaints as the knowledge of the presence of an abdominal tumor, pressure symptoms upon the bladder or rectum, gastrointestinal disturbances, feeling of weight in the pelvis, and symptoms associated with relaxed vaginal walls and prolapse.

Another interesting point may be expressed in a study of the following table which brings out the relationship between the presence of menorrhagia and the size of the tumors encountered (Table I).

TABLE I

SIZE	WHITE		COLORED	
	MENORRHAGIA	NO MENORRHAGIA	MENORRHAGIA	NO MENORRHAGIA
6 to 8 weeks' pregnancy	25	13	1	3
3 to 6 months' pregnancy	20	10	12	8
Over 6 months' pregnancy	1	0	4	3

Although our study revealed only three women in this group who had a definite complaint of sterility, a résumé of the parity of the patients here presented may be worth noting. Of the nulliparous women in this list, four were unmarried (Table II).

TABLE II

GRAVIDA	PARA	NUMBER
0	0	35
i	0	4
i	i	13
ii	0	4
ii	i	5
ii	ii	22
iii	0	1
iii	ii	2
iii	iii	7
iv	i	1
iv	ii	1
iv	iii	1
iv	iv	2
v	iv	1
vi	iii	1

The age incidence in this group might also prove of some interest, the ages ranging from twenty-three to fifty-three years (Table III).

TABLE III

AGE	WHITE	PERCENTAGE	COLORED	PERCENTAGE
Under 25 years	1	1.4	3	9.6
25 to 35 years	6	8.7	9	29.0
35 to 45 years	37	53.5	13	42.0
Over 45 years	25	36.4	6	19.4

DISCUSSION

An analysis of the statistical data presented above may throw some light on the various factors which have been credited with providing inertia for the growth of fibromyomas. Witherspoon and other authors have brought to our attention the relative frequency of the simultaneous presence of fibromyomas, adenomyosis, and hyperplasia of the endometrium. This, together with the large number of patients in his series displaying cystic oophoritis and salpingitis, strengthened his hypothesis of hyperestrinism as the important etiologic factor in the stimulation to growth of fibromyomas. A correlation of our findings will be undertaken in an effort to evaluate this theory.

The frequency of cystic oophoritis in our series is much less than that found by Witherspoon⁴ and Häggström,¹⁰ this group having only a 13 per cent incidence discoverable grossly or microscopically. Salpingitis was present in twenty-six, or 83.8 per cent, of the colored women and only three, or 4.33 per cent, of the white. It must be remembered that 100 per cent of these patients had uterine fibromyomas while 63.7 per cent of the white women and 25.8 per cent of the colored showed evidences of adenomyosis, either the subbasal or true types, and 13 per cent of the white women had external adenomyosis (endometriosis), this latter entity being entirely absent in the colored patients studied. Hyperplasia of the endometrium was present in 53 per cent of our patients, 49.1 per cent of the white women and 60.6 per cent of the colored showing evidence of this type of pathology.

Witherspoon, after studying a group of colored women who had almost 100 per cent salpingitis and cystic oophoritis in association with fibromyomas, claimed that the pelvic inflammatory process brings an increased blood supply to the pelvis, producing an increased ovarian activity with hyperestrinism. The atretic follicles thus produced defeat the possibility of corpus luteum formation and an excess of estrogenic principles results. This may be a factor in the production of fibromyomas in the colored patients in this series, the majority of whom had coexisting salpingitis, but Witherspoon further deduces that the same etiologic factors are active in producing adenomyosis, a condition that was relatively rare in our colored patients but common in the white women who had no evidences of pelvic inflammatory disease. This becomes increasingly difficult to understand since the colored women had, as a rule, larger tumors, a fact that would suggest a greater excess in the circulating active estrin content.

Again, if hyperplasia of the endometrium can be taken as a criterion of excessive estrin stimulation, one would expect to find more than a 53 per cent incidence in a series of patients with fibromyomas. In postmenopausal patients with theca or granulosa cell tumors of the ovary, bleeding from the uterus is frequently encountered. These

patients have a hyperplasia of the endometrium as a result of the hyperestrinism produced by or in the tumor. Since hyperplasia of the endometrium is induced by estrogenic principles in the presence of these ovarian neoplasms in patients who have passed the climacteric, it is difficult to understand the comparatively large number of post-menopausal patients in the present series having endometrial atrophy of the menopausal type in the presence of fibroids which are products of estrin stimulation.

Some observers make much of the absence of corpora lutea in the presence of fibromyomas on the theory explained above. Häggström found many ovaries in his series to contain these bodies in various stages of development and retrogression. In our group nine patients showed the presence of corpora lutea, recent or old, in the ovaries removed, and, if we may be allowed to presume, there were probably many more in the ovaries left in situ which were not mentioned in the operative records.

A study of the symptomatology gives rise to some interesting thoughts. There were 61 patients in this series who had menorrhagia; 49 of these had submucous fibromyomas with or without adenomyosis and 12 had subserous and intramural tumors. If the estrogenic factor is so potent as to produce hyperplasia of the endometrium with a resultant bleeding in elderly women with hormone producing tumors of the ovary, we are forced to inquire as to why the same stimulus that produces the fibroid tumors does not develop menorrhagia in more than 61 per cent of our patients.

The estrogenic principle is the active motor stimulant for the uterine musculature and some workers attempt to explain dysmenorrhea seen in patients with fibromyomas on a hyperestrin basis, the excess of this hormone providing for vigorous uterine contraction unopposed by progestin because of the suppression of the corpora lutea. In our group 42 patients complained of pain associated with the menstrual periods. Of this number, 27 had submucous fibromyomas, 15 had subserous and intramural tumors and 14 had salpingitis, which factor alone is frequently responsible for dysmenorrhea because of the pelvic and bowel adhesions resulting from this type of pathology. Looking deeper into this symptomatic element, it can be seen that the majority of patients with menorrhagia and dysmenorrhea had submucous fibromyomas, while a lesser number displayed subserous and intramural growths. We feel with Häggström that the location of the tumors with respect to their proximity to the uterine cavity is a more logical explanation for the menorrhagia and dysmenorrhea, the bleeding resulting from a constant endometrial hyperemia induced by the tumors directly underlying and crowding the endometrium and the dysmenorrhea as a product of vigorous uterine contraction in an attempt to expel the

foreign bodies (tumor masses) lying in or near its cavity. By the same token patients with very large subserous and intramural fibromyomas which may reach full-term pregnancy proportion are lacking in these symptoms.

A survey of the obstetric histories in this group shows that there was sterility in forty of the women, four of the nulliparas having been unmarried. Still, we are dealing with a series of patients in whom salpingitis of one form or another with tubal closure was present twenty-nine times, a fact accounting for some of the lack of pregnancy. Again, we must disagree with Witherspoon's contention that the sterility associated with fibromyomas is explained totally by the hyperestrinism he believes is produced by the atretic follicles in the absence of corpora lutea. We cannot believe that a great number of the sterilities in this group can be explained upon a basis of estrogenic excess because of the small number of our patients displaying atretic follicles and because of the occasional presence of corpora lutea.

SUMMARY

A study of the uterine walls, ovaries, and endometria in a series of 100 patients having fibromyomas with a correlation between these findings and the clinical histories and symptoms, still gives us no definite basis upon which to make an absolute statement as to a single etiologic or stimulating factor in the production of fibromyomata uteri, adenomyosis externa or interna, and hyperplasia of the endometrium with resultant menorrhagia, dysmenorrhea, or sterility.

Evidence in favor of Witherspoon's theory making hyperestrinism the single activator in the production of these pathologic and clinical entities, can be found in the observation of the rapid growth of fibromyomas during pregnancy and their puerperal and menopausal regression. Such facts follow very closely the estrin levels now well established, as does the discovery of hyperplasia of the endometrium associated with the presence of theca and granulosa cell tumors of the ovary in women who have passed the menopause.

We have presented in our discussion factors that may tend to oppose this theory, at least in part. We must, therefore, feel with Witherspoon that hyperestrinism plays a part in the production of the changes herein studied and discussed, but we cannot be convinced that it is the sole agent because of the lack of consistency in the finding of other pathologic and symptomatologic entities in association with fibromyomas.

The logical conclusion that can be derived from this study is that fibromyomata uteri, endometriosis, adenomyosis uteri, and hyperplasia of the endometrium with associated menorrhagia, dysmenorrhea, and sterility cannot be traced to a single etiologic agent but appear to be products of various and varying factors.

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- (1) *Meyer, Robert*: The Pathologic Anatomy of the Uterus, Chap. 7, p. 213.
 (2) *De Snoo*: J. Obst. & Gynec. Brit. Emp. 41: 568, 1934. (3) *Graves, William P.*: Uterine Myomata. In System of Obstetrics and Gynecology by Curtis, Philadelphia, 1933, W. B. Saunders Company 2: p. 745. (4) *Witherspoon, J. Thornwell*: Endocrinology 17: 703, 1933. (5) *Idem*: Surg. Gynec. Obst. 56: 1026, 1933. (6) *Idem*: Surg. Gynec. Obst. 58: 57, 1934. (7) *Idem*: Surg. Gynec. Obst. 61: 743, 1935. (8) *Cullen, Thomas E.*: Cancer of the Uterus, New York, 1900, D. Appleton and Company, p. 479. (9) *Novak, Emil, and Martzloff, Carl H.*: AM. J. OBST. & GYNEC. 8: 385, 1924. (10) *Hüggström, Paul*: Ztschr. f. Geburtsh. u. Gynäk. 102: 36, 1932.

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DISCUSSION

DR. HAROLD O. JONES.—I believe that hyperplasia of the endometrium is a term that is often very carelessly used. Certainly the sections thrown on the screen could be classified as different phases of cyclic manifestation. I have the same criticism of Witherspoon's work and do not believe that he is justified in making comparisons unless sections from both ovaries are available for study of the corpus luteum.

DR. RALPH A. REIS.—Dr. Baer, Dr. DeCosta, and I undertook a study similar to this one of one thousand consecutive patients at Michael Reese Hospital, two or three years ago. Although Witherspoon found salpingitis in almost 100 per cent of his series, we found it in only 19.4 per cent, which is even lower than Dr. Kanter's figures. These variations are probably due to the differences in the social, economic, and racial status of these series of patients. We found also very little sterility, over 80 per cent of our patients having been pregnant one or more times. In patients who were sterile, there was a 31 or 32 per cent incidence of salpingitis, whereas in those who had had children the incidence was only 7 per cent. We thought, therefore, that the sterility was due to associated salpingitis and not due to the fibroid.

We have tried to be very rigid in our description of hyperplasia of the endometrium and accordingly found hyperplastic endometrium in less than 18 per cent of the patients whose uteri were examined. The lack of symptoms in as large as 30 per cent, as Dr. Kanter reported, corresponds with our figures of 32 per cent which showed neither bleeding nor pain nor increase in menstruation.

DR. AARON E. KANTER (in closing).—I expected a little controversy about what is to be considered hyperplasia. That is the reason I stated what stage of the endometrium we studied. I believe that dilated glands of varied sizes, especially with duplication of glands, is not a normal finding. Some of the slides shown tonight were hyperplasia but it is difficult to state the type.

We have not tried to bring out conclusively the cause of fibromyomas, but we do not believe it is an excessive amount of estrogenic hormone in the system.

Huffman, J. W.: *Trichomonas Vaginalis Vaginitis*, Am. J. Surg. 30: 312, 1935.

This is a preliminary report on 14 patients suffering from vaginitis, associated with *Trichomonas vaginalis* infestation, who have been treated with iodochlorhydroxyquinoline. The use of this product appears more satisfactory in this group than any other previously tried method. In the patients under observation there have been no recurrences up to five months.

J. THORNWELL WITHERSPOON

SOME POINTS IN THE TREATMENT OF ENDOMETRIAL HYPERPLASIA BY PROGESTERONE THERAPY*

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THE treatment of menstrual disorders and ovarian dysfunction by methods of ovarian organotherapy has in the past been notoriously unsatisfactory and inefficient. This has been due to a variety of reasons. Lack of knowledge of the exact processes involved was, of course, an important factor. Furthermore, the various ovarian preparations used for therapeutic purposes could not be anything but ineffectual in securing the desired results. We now know that extracts of the corpus luteum, ovarian residue, and such, when given by mouth, are practically valueless, while those formerly administered by hypodermic injection contained little or none of the potent hormones.

The isolation and purification of the two important ovarian hormones, estrin and progesterone, have led to renewed hopes from the therapeutic standpoint. True, our knowledge of ovarian function has advanced greatly, and the nature and function of the ovarian hormones are better understood, so that it is possible now to approach the study of patients presenting menstrual abnormalities in a more logical manner, and in some instances at least to offer more rational treatment than has hitherto been possible.

At the same time we would emphasize that the indiscriminate injection of ovarian hormones in the treatment of menstrual disorders can result only in many bitter disappointments. In considering the two ovarian hormones, estrin and progesterone, it must be recalled that while the action of progesterone succeeds and is complementary to that of estrin in the normal cycle, at the same time the effects of the two are also antagonistic to each other to a degree. These facts can be taken advantage of in ovarian therapy, and the relations between the two must be constantly kept in mind if we wish to treat our patients on rational lines. For example, in the patient whose ovaries are already producing an oversupply of estrin, it would be most illogical to administer more of the already too abundant hormone, while on the other hand, in the case of an underproduction of progesterone, this can be compensated for only by the administration of progesterone and not estrin.

*Read, in part, by invitation, before the New York Obstetrical Society. February 11, 1936.

It is not our purpose here to go into the whole question of ovarian therapy but rather to emphasize some points which have developed in the treatment of a group of patients by progesterone therapy. This group includes several women presenting themselves on account of persistent and profuse uterine bleeding, in whom, after curettage, the typical microscopic picture of endometrial hyperplasia was revealed. The basis for this type of benign bleeding would appear to lie in the failure of ovulation to occur and the consequent failure of the corpus luteum to develop. There is thus probably a persistent estrin activity with little or no production of progesterone. This group would, therefore, appear to be logical subjects for progesterone therapy in the hope of supplying their deficiency. As the fundamental factor is the failure of ovulation to occur, a still more logical treatment would be the administration of the ovulation-stimulating hormone of the anterior pituitary, which is clinically not yet possible.

The first difficulty encountered in progesterone therapy is the estimation of the dosage to be used. Unfortunately there is at present no satisfactory means available for determining the progesterone content of the blood in small amounts. Furthermore, although it is possible to determine the progesterone content of corpora lutea in the laboratory, we are entirely ignorant of the amount of hormone produced daily during the period of activity of a particular corpus luteum. Consequently, although we may recognize that in the given case there is deficient production of progesterone, we have no means available for learning what the deficit actually is. For this reason the initial dosage used can only be decided empirically, the dosage being increased or decreased, or the treatment continued or suspended according to the results obtained.

The following examples of uterine bleeding associated with endometrial hyperplasia are presented in some detail as they illustrate certain particular points in connection with progesterone therapy in this type of bleeding. The progesterone used was the purified hormone prepared from sows' ovaries by one of us (Elden) according to the method of Allen and Meyer, the hormone being then dissolved in sesame oil, and standardized.*

CASE 1.—E. C. (Unit 11752), aged forty-six, para i. The patient was admitted in June, 1933 after several weeks of rather persistent bleeding, at times moderately profuse. Diagnostic dilatation curettage June 16, 1933; curettings showed a moderate degree of hyperplasia. Following dilatation and curettage there was normal menstruation for five months, then she began to have persistent slight bleeding, the amount never great but became of such a nature that there were only two or three days free from bleeding in each month. Antuitrin-S was tried on several occasions without success. Total period of this slight bleeding was one year. She had associated sinus headache. Radiation therapy or hysterectomy was being

*One rabbit unit corresponds to 1 mg. of the purified crystalline hormone.

considered. Progesterone $\frac{1}{25}$ Rb.U. Dec. 7, 9, 11, 1934 (total $\frac{3}{25}$ Rb.U.). Bleeding stopped twentyfour hours later, slight recurrence for one day, then stopped entirely for twelve days, the longest period of freedom in over a year. Slight bleeding began again, increased in amount until it amounted to what was apparently a moderately profuse menstrual period, duration twelve days. Without further therapy, she menstruated quite normally, at twenty-eight- to thirty-day intervals, duration four to five days, until September, 1935 when she began to have irregular two- to three-day periods of slight bleeding in between regular menstrual periods. With establishment of regular menstruation, the previously persistent headaches disappeared and recurred only at time of menstruation. She was treated again in November, 1935 on account of recurrence of slight bleeding. She was given $\frac{2}{25}$ Rb.U. on 3 successive days (total $\frac{6}{25}$ Rb.U.) This second period of therapy was in turn followed by improvement and reestablishment of normal menstruation.

CASE 2.—R. A. (Unit 45142). This patient was first admitted on Nov. 16, 1931, at the age of sixteen years. At the age of thirteen, one year after onset of menstruation, she began to bleed persistently and almost daily up to the time of this admission, usually slight but at times quite profuse and for the past two months constant, rather free bleeding. Secondary anemia, Hb. 70 per cent. Dilatation and curettage Nov. 19, 1931, typical hyperplasia. Dilatation and curettage was followed by 3 small x-ray treatments (105 m.a. each, ovaries, spleen, pituitary). She was slightly relieved by above treatment, but in a few months there was a recurrence of bleeding, usually not profuse but so persistent that the free intervals were infrequent and of short duration. Readmitted Jan. 31, 1935, aged twenty, after an episode of rather profuse bleeding. Basal metabolism rate -10 per cent. Given $\frac{5}{25}$ Rb.U. on each of 3 successive days (total $1\frac{1}{25}$ Rb.U.). Bleeding decreased second day and had practically stopped on third day. After six days' freedom from bleeding, $\frac{5}{25}$ Rb.U. repeated three days later (total $1\frac{1}{25}$ Rb.U.) no bleeding, the last 2 doses probably unnecessary. No bleeding for slightly over five weeks, the longest interval of freedom in past four years. Slight bleeding then began and persisted, occasionally somewhat increased. After three weeks given $\frac{2}{25}$ Rb.U. on three successive days (total $\frac{6}{25}$ Rb.U.) flow decreased but did not stop, amount very moderate. A week later 3 doses $\frac{2}{25}$ Rb.U. at two-day intervals. Bleeding stopped entirely and did not recur for three weeks. Slight bleeding then began May 6, 1935. Given $\frac{2}{25}$ Rb.U. on three successive days (total $\frac{6}{25}$ Rb.U.), bleeding stopped temporarily but recurred, and repeated 3 doses of $\frac{2}{25}$ Rb.U. beginning three days after last series (total $\frac{6}{25}$ Rb.U.). A very slight daily flow persisted for a total of four weeks, only on two days amounted to as much as a normal menstrual period. Given $\frac{4}{25}$ Rb.U. on three successive days (total $1\frac{2}{25}$ Rb.U.). Bleeding stopped entirely after third dose. No bleeding for three weeks. Bleeding began again on June 24, 1935, rather free. Three daily doses $\frac{4}{25}$ Rb.U. (total $1\frac{2}{25}$ Rb.U.). Bleeding decreased and finally stopped after three days. Thirty-one days' freedom from bleeding except for slight spotting on one or two occasions. Bleeding began again July 31, 1935, and was rather profuse. Two doses $\frac{4}{25}$ Rb.U. (total $\frac{8}{25}$ Rb.U.); did not report for other dose. Flow decreased but increased markedly a week later, given 2 doses $\frac{6}{25}$ Rb.U. (total $1\frac{2}{25}$ Rb.U.); flow stopped six days later; duration of flow sixteen days. No bleeding for thirty days, followed by free flow for ten days, given 4 doses ($\frac{4}{25}$ Rb.U., total $1\frac{4}{25}$ Rb.U.). Flow checked after second injection but persisted for several days more before stopping entirely. This patient presented difficulties in regularity of treatment. She felt so much better than at any time in the previous four years that she became at times rather perfunctory in reporting symptoms. No treatment given since September, 1935. No bleeding in October except for very slight flow

for about an hour on 2 occasions. Began to flow Nov. 1, 1935, duration one week, very profuse for three days. Nothing in the way of a regular period in December, but has had slight bleeding for part of a day on three occasions.

CASE 3.—N. G. (Unit 98540), aged eighteen, single. The patient was admitted in January, 1935 on account of excessive menstruation. Menstrual onset at age of twelve, and quite normal for first four years. Since pneumonia two years ago menstrual periods totally irregular at four-to fourteen-day intervals, scanty in amount and of variable duration from two to eight days. Had received thyroid therapy from family physician, amount unknown. Had gained 10 pounds in weight in past five months. Physical and pelvic examinations essentially negative, the only significant finding being a basal metabolism rate of -16 per cent. Dilatation and curettage Jan. 31, 1935 showed typical endometrial hyperplasia. Following dilatation and curettage given $\frac{3}{25}$ Rb.U. of progesterone weekly for three weeks (total $\frac{9}{25}$ Rb.U.), also $\frac{1}{2}$ gr. of thyroid daily. No bleeding for two months, then had apparently normal menstrual period lasting six days. For four months was given $\frac{3}{25}$ Rb.U. of progesterone in last half of each twenty-eight-day cycle, 4 normal periods occurring after this treatment.

All therapy then was suspended and for past three months there had been no bleeding of any kind. Associated with this amenorrhea she developed symptoms of a mild hypothyroidism, and a recent basal metabolism rate gave a reading of -21 per cent. She is at present receiving thyroid therapy, 3 normal menstrual periods resulting, the last, January, 1936.

CASE 4.—B. A. (Unit No. 79071), aged nineteen, single. The patient was admitted on Aug. 22, 1933 on account of vaginal bleeding. Menstrual onset at age of thirteen, irregular and scanty for three years followed during the next two years by more normal menstrual flow though somewhat irregular. Beginning a year before admission, duration of menstrual period fourteen days, and for past six months bleeding has been almost constant. Has lost 40 pounds in weight in past year by dieting, present weight 73.2 K. General physical and pelvic examinations essentially negative. Laboratory findings showed an R.B.C. of 2,760,000; Hb. 55 per cent; W.B.C. 6,100. Basal metabolism rate -1 per cent. Blood chemistry normal; galactose tolerance test normal. Dilatation and curettage Aug. 26, 1933, typical endometrial hyperplasia. Treated for next three months by anterior pituitary gland given in salol coated capsules at theoretical time of ovulation with no benefit. Injection of 200 units of antuitrin-S was also done without benefit; irregular and persistent bleeding continued. Second dilatation and curettage Dec. 9, 1933, typical endometrial hyperplasia. Given a total of 10 Rb.U. progesterone in three days just after theoretical time of ovulation, and this was repeated at the same time and in the same amount in 2 succeeding cycles. Three periods of bleeding (menstrual?) occurred, rather profuse and of six to seven days' duration, no bleeding between these periods.

A control period now started with no therapy. No bleeding of any kind for two months followed by a normal period of six days' duration. Two weeks later began to bleed again and this continued for twenty-four days. Two normal periods occurred in the succeeding two months. For the next four months, the periods were irregular, profuse, and when not bleeding actively, there was almost daily "spotting." Several endometrial biopsies taken during the control period showed no premenstrual changes. Urinary estrin studies showed varying amounts of estrogenic substance from 0 to 32 Rb.U. daily.

Third dilatation and curettage on Feb. 24, 1935. Following this operation, she was given small doses, $\frac{3}{25}$ Rb.U., of progesterone at weekly intervals during the last half of her menstrual cycle, and this was continued for the next eight months.

Menstrual periods have been regular to within a day or two, while the duration and amounts of flow have been normal. Treatment stopped in October, 1935. After two essentially normal menstrual periods, began to "spot." Progesterone $\frac{3}{25}$ Rb.U., weekly, has apparently again brought the situation under control.

CASE 5.—B. B. (Unit No. 93258), aged thirty-two. The patient had a spontaneous miscarriage at six months three years ago. Dilatation and curettage August, 1934 on account of menorrhagia, moderate hyperplasia, followed by period of relief. Recurrence of menorrhagia in March, 1935 increasing in amount and duration; periods regular but very profuse and lasting six to seven days. Progesterone therapy began in June, 1935. Two doses of $\frac{3}{25}$ Rb.U. on two successive days before onset of periods each month since that time have resulted in periods of normal duration and amount.

In addition to the foregoing patients whom we have observed for considerable periods of time, a number of others have been treated for shorter periods of time. Some of them may apparently be regarded as successes though the period of observation has been too short to be assured of this. There have also been a number of failures. These latter we are inclined to attribute to either too small dosage or to improperly timed dosage. We hope to present a more complete series at a later date.

DISCUSSION

The results obtained in the treatment of these five cases of vaginal bleeding can be regarded as satisfactory, but the mechanism, by which these results were brought about, is not so clear. These patients presented varying degrees of uterine bleeding and were treated on the assumption that their own production of progesterone was deficient. As mentioned above, it is at present impossible to determine the degree of deficiency of progesterone production in the individual, consequently the dosage administered has been determined on empirical lines. The small dosage was selected for no particular reason except as a starting point.

Case 1 presents an extraordinary result obtained from a very small dosage of progesterone. The immediate effect so far as the bleeding was concerned was striking enough, but of still more interest was the ensuing period of normal menstruation without further therapy. One can only speculate as to the mechanism by which this was brought about. It might appear that the small doses of progesterone were in this instance sufficient to bring about a balance between the estrin and progesterone production on the part of the organism and that that balance once restored was maintained by the organism for a period of several months. That the result obtained was not a matter of simple coincidence is demonstrated by the fact that the slight recurrence of symptoms nine months later was again controlled by the same therapy with small doses of progesterone.

In Case 2 the situation was somewhat different, repeated administration of progesterone being necessary from time to time to control the bleeding, and also somewhat larger doses were found to be necessary to bring about the desired result. As will be seen above in her case history, while small doses totalling $\frac{9}{25}$ Rb.U. of progesterone caused a decrease in the bleeding, usually $1\frac{1}{25}$ to $1\frac{1}{25}$ Rb.U.

were necessary to bring about complete control. The picture here is more nearly what one would expect in frank substitution therapy. The end-result and her behavior during three months without any therapy suggest that for the time being at least a proper balance between estrin and progesterone production may have been established.

In Case 3 we are dealing with the combination of uterine bleeding associated with endometrial hyperplasia and also a very definite hypothyroidism. The beneficial results of progesterone therapy are seen in the 5 normal menstrual periods which occurred after its use preceding each period. This in turn has been succeeded by very definite signs of hypothyroidism.

Case 4 presents still different aspects. Following treatment with large doses of progesterone, some tendency toward periodicity was established, but the three periods, thus treated, were profuse and of longer than normal duration. This effect is difficult to explain, and we can only speculate on the mechanism by which the effects were produced. The results were certainly not as striking as in the preceding cases with the administration of smaller dosage, and in this patient too the situation was brought under control later by the repeated administration of small doses of progesterone. Possibly the latter procedure more nearly simulates the normal situation in the body in regard to progesterone production.

Case 5 may be regarded as an example of severe menorrhagia controlled, though as yet not cured, by progesterone therapy.

It is obviously impossible to draw any sweeping conclusions from the above series, and no attempt will be made to do so. From the results obtained, however, it would appear that treatment by progesterone therapy may well be given serious consideration in the treatment of uterine bleeding associated with endometrial hyperplasia when there is presumably a deficient production of progesterone on the part of the ovaries. If and when it shall become possible to determine how much of the hormone is necessary for normal function and to determine how much is produced by the individual in a given case, it will then be possible to determine the dosage according to the deficit which exists. For the present, however, the dosage will have to be along empirical lines until we learn in a given case, by the method of trial and error, the amount necessary to establish equilibrium. Another fact to keep in mind is the fact that solutions in oil are absorbed slowly. Consequently no immediate effect would be expected; at least twenty-four to forty-eight hours must elapse. This is of importance in arranging the time of administration of the hormone.

The dosage in our patients has been very small when compared with the dosage found necessary for frank substitution therapy in experimental work. Thus, Allen and Corner found it necessary to administer 1 Rb.U. per day to maintain pregnancy in the castrated rabbit. Kaufman, in an interesting experiment on a castrated woman, found it possible to reproduce a premenstrual endometrium followed by bleeding only after the administration of 50,000 rat units of progynon followed by 35 rabbit units of progesterone. Elden, repeating his experiment, failed to bring about similar changes through using the

same dosage of ovarian hormones. All these experiments indicate the large amounts of ovarian hormones necessary for frank substitution therapy, and the small dosages used in our patients obviously do not fall in that category. Kaufman has also had success in treating patients similar to ours with relatively small doses of progesterone, 5 to 10 rabbit units extended over five-day periods, though his dosage is somewhat larger than we found necessary.

The explanation of the results obtained is not clear, and we can only theorize as to how they were brought about. Obviously with the ovaries in situ, the situation is quite different from that of the castrated woman.

Possibly a certain amount of progesterone is produced even in the absence of ovulation in follicles undergoing atresia. Or possibly the effect produced by these small doses is an indirect one on the cycle through the medium of the pituitary rather than from any direct effect on ovaries or uterus. The question cannot be answered at the present time but offers an interesting problem for future investigation.

SUMMARY AND CONCLUSIONS

The results obtained in five women presenting uterine bleeding as sociated with endometrial hyperplasia and treated by progesterone therapy are presented. In this small series the results may be regarded as satisfactory, but they are also presented on account of the problems arising in connection with the determination of the proper dosage to use, which for the present must be along empirical lines, as well as the possible explanation of the results obtained. The correlation of the appearance of the endometrium with the therapy, by means of frequent biopsies, would have been highly desirable, but unfortunately it was not feasible.

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The author reports his second case of undescended ovary. The usual symptom is pain which is localized at the area of attachment. In this case the pain appeared to result from the spill of blood. The location is likely to be in the iliac fossa but may be higher. The gonad is prone to be covered by the colon but may lie laterally to it.

There is no need to remove the ovary, but its nerve supply should be severed.

H. CLOSE HESSELTINE.

CERVICAL DILATATION IN DRY LABOR AND AFTER DELIBERATE EARLY RUPTURE OF THE MEMBRANES*

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HOW does the cervix open, and what is the rôle of the amniotic sac in labor, are questions that have been disputed since the beginning of scientific obstetrics.

The opinion that the membranes are vital to labor goes back, according to Jaquemier,¹ to the teaching of Paré's pupil, Guillemeau, who lived in the latter half of the sixteenth century. It is also known that harsh criticism followed the pioneer daring in 1738 of Mary Donally, an English midwife, who was probably the first to induce labor by rupturing the membranes.² She achieved the delivery of a premature but live child through a contracted pelvis that had caused the death of two previous full-term infants. A Dr. Macaulay could not be dissuaded by a consultation of his colleagues in 1756 from the same course, which had a similar happy termination.³

William Smellie⁴ in 1752 cautioned against rupture of the membranes, but stated: "The membranes appear to play no part in labor except to hold in the water necessary for lubrication. Dilatation is effected by the head." The then prevalent hydrostatic wedge theory was upheld by Thomas Denman⁵ who in 1778 made the oft-quoted statement: "The amniotic fluid enclosed in the membranes procures the most gentle, efficacious dilatation of the os uteri." However, he admitted that "in many cases the membranes break spontaneously before the period of complete dilatation without any material inconvenience." Baudelocque⁶ in 1789 held a gloomy prognosis for dry labor (even though he ruptured the membranes for induction). However, he warned the profession that "dilatation is not immediately and entirely the effect of that species of wedge." John Burns⁶ at the turn of the century stated that he "could not go the length of some who say the evacuation of the waters is always hurtful for there are circumstances in which it is allowable and beneficial." But he went on to strike the first blow against "meddlesome midwifery."

In 1806 William Potts Dewees was graduated from the University of Pennsylvania. His thesis, which Howard A. Kelly quoted Shippen as saying marked a new era in the history of medicine, was "An Essay on the Means of Lessening Pain and Facilitating Certain Cases of Difficult Parturition," in which he criticized the theorizing of Denman. The following year he continued his criticism in editing Heath's translation of Baudelocque, the first textbook of obstetrics published in the United States. Shortly afterward appeared his classic *Compendious System of Midwifery*.

Dewees⁷ pointed out that, if the membranes were a dilating wedge, they must be stronger than the cervix, and he compared the ease with which the membranes rupture at the slightest touch to the difficulty of manual dilatation. Again, in the absence of membranes, labor should be almost impossible or very difficult, which he found "contrary to experience" in spite of occasional exceptions.

Dewees' explanation of the "Manner in Which the Os Uteri Is Opened" is briefly that the cervix begins to lose thickness and breadth as soon as it is operated

*Read at a meeting of the Cincinnati Obstetrical Society, March 12, 1936.

upon, this in spite of the circular muscles. The longitudinal muscles contract coincident with the relaxation of the circular muscles, and the cervix is thus gradually retracted over the head.

Faced thus with two entirely different theories to explain the mechanism of the dilatation of the cervix, succeeding obstetricians hesitated to fly in the face of tradition and tried to combine the two. For example, Velpeau felt that although Dewees' explanation was correct, the waters helped "somehow" in the process, and he called for new studies on the subject. Jacquemier's textbook of 1846 considered that rupture of the membranes in no way hindered dilatation. In 1858, Sinclair and Johnston⁸ noted that in 13,000 deliveries at the Dublin Lying-In Hospital, the rupture of the membranes during the first stage did not tend to delay labor, and they reported "no hesitancy in puncturing them." On the other hand, Chailly pleaded for the membranes if only as a protection to the child. Ramsbotham in England, Cazcaux in Paris, and the then rising German school ignored Dewees, and although Gunning S. Bradford taught his theory in 1861, even America, led by Hugh L. Hodge, condemned it to the place of historical interest.

Although our textbooks teach the hydrostatic wedge theory with or without minor modifications, impetus to a new study of the mechanism of the dilatation of the cervix has come from two sources: first, the increasingly popular method of inducing labor by rupture of the membranes, and second, the apparently independent evolution of the Dewees explanation, and a practical application of it, by Kreis of Strasbourg.⁹

In accordance with the hypothesis that the membranes are the dilating agent or at least the most significant element in the dilatation of the cervix, dry labor, as a corollary, should be exceedingly difficult and prolonged. With the theory of reciprocal muscle action as the dilating mechanism, the presence or absence of the membranes should be immaterial. In fact, the absence of membranes should aid labor inasmuch as the retraction of the cervix is more easily accomplished over a hard head than over a somewhat yielding mass of fluid. As a test of the validity of either of the two explanations, a very simple experiment might be devised to determine the length and difficulty of labor in relation to the integrity of the amniotic sac.

Supplementing observations reported in 1934 of the results obtained with deliberate rupture of the membranes early in labor,¹⁰ the problem was again investigated with the material of 1,621 obstetric admissions to the Methodist Episcopal Hospital of Brooklyn during the year 1934 and 1935. To have an adequately controlled experiment all variable factors have to be eliminated. Hence, the study was limited to strictly normal parturitions by excluding the following: abortions, premature labors (to thirty-eight weeks), breech and transverse presentations, twins, hydramnios, toxemia, bleeding cases, contracted pelvis, and constitutional complications, such as tuberculosis and heart disease. It was felt wise to exclude women admitted to the hospital in the second stage of labor, as well as those whose charts contained insufficient data for proper classification. There was a fourth cause for exclusion, namely, ignorance of whether or at what time the membranes actually ruptured. In none

of the recent studies on dry labor has this been recognized, and undoubtedly the membranes were erroneously considered intact. The size of the error thus introduced is considerable. In the Woman's Clinic of the New York Hospital¹¹ where such a classification is made, the number of cases with time of rupture undetermined amounts to about 10 per cent. At the beginning of this experiment some 11 per cent of women fell into this group, but by the routine use of the brom-thymol-blue test during the last few months, the figure was reduced to 6 per cent.

TABLE I. CLASSIFICATION OF OBSTETRIC ADMISSIONS, METHODIST EPISCOPAL HOSPITAL, BROOKLYN, N.Y. JULY 1, 1934 TO JUNE 15, 1935

	COMBINED	PRIVATE	WARD
All obstetric admissions	1621	723	898
Abnormal cases	354 (22%)	169 (23%)	185 (20%)
Admitted in second stage	117 (7%)	54 (7%)	63 (7%)
Insufficient data	36 (4%)	22 (3%)	58 (6%)
Undetermined rupture of the membranes	91 (6%)	61 (8%)	30 (3%)
<i>Normal Cases for Study:</i>	1001	403	598
A. Intact membranes	404	194	210
B. Dry labor	311 (31%)	130 (32%)	181 (30%)
C. Spontaneous "partial dry"	107 (11%)	38 (9%)	69 (12%)
D. Deliberate "partial dry"	179	41	138

There were thus 1001 normal, full-term, occipitoanterior or occipitoposterior deliveries available for the experiment, as indicated in Table I. These were grouped into four classes: A, typical labor with intact membranes to the end of the first stage, that is, those cases in which dilatation of the cervix might have been accomplished by the hydrostatic wedge; B, typical dry labor, that is, those women whose dilatation was accomplished in the complete absence of the hydrostatic wedge, presumably by the reciprocal muscle action; C, termed spontaneous "partial dry" wherein the membranes ruptured spontaneously after a dilatation of from 4 to 7 cm.; D, the experimental group, women in active labor with a dilatation of from 4 to 7 cm., on whom deliberate rupture of the membranes was practiced in order to observe whether the absence of a hydrostatic wedge made any difference in the type of labor and whether there was any difference in the early and later parts of labor. For most purposes Classes C and D can be combined under the heading of "partial dry labor."

A very striking finding was the high incidence of dry labor, 31 per cent, which included, however, rupture of the membranes up to the establishment of pains at twenty-minute intervals. Williams¹² has no

TABLE II. DISTRIBUTION OF PRIMIPARAS AND OCCIPITOPOSTERIOR POSITIONS

	A	B	C, D
All cases, 1,001 (100%)	40%	31%	29%
All prim., 484 (100%)	35%	35%	30%
Prim. in each class	42%	54%	51%
All o-p's, 381 (100%)	39%	29%	31%
O-p's in each class	37%	36%	41%

statistics of his own but quotes a figure of 10 per cent. At the New York Hospital¹¹ the incidence in normal vertex cases is 19 per cent with another 10 per cent unclassified. Of the two conditions usually blamed for this accident, namely, contracted pelvis and occipitoposterior position, Schultze¹³ showed definitely that contracted pelvis was not a factor, the nineteenth century writers to the contrary notwithstanding. Table II demonstrates that occipitoposterior position is also not a predisposing factor. On the other hand as has been pointed out by others, a tendency to premature rupture is apparently associated with primiparity.

Returning to the mechanism of dilatation of the cervix, it is apparent that, as the textbooks state, the absence of a fluid wedge should lead to

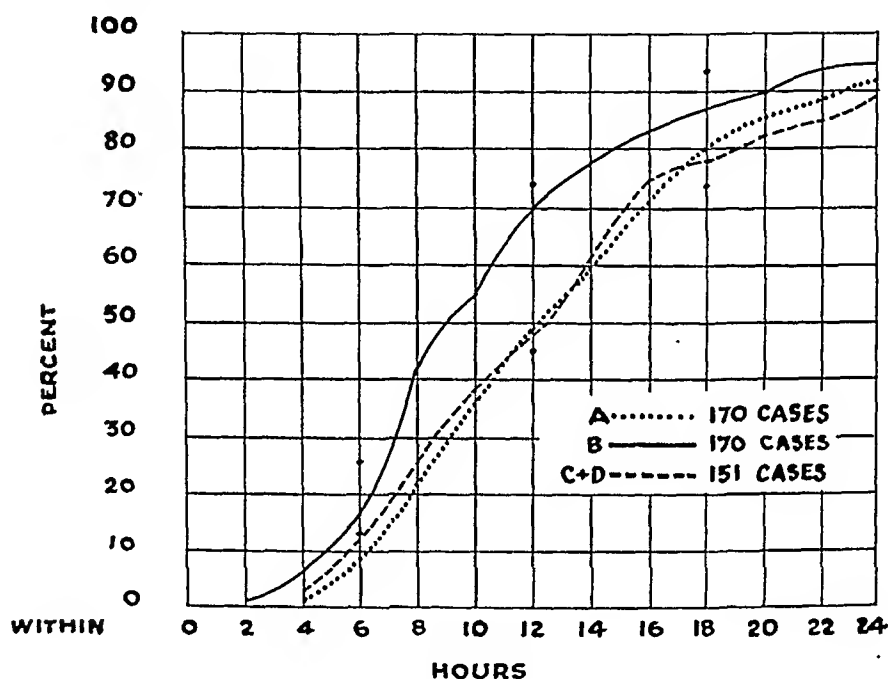


Fig. 1.—Ogive of labors completed, primiparas.

a prolonged labor. On the other hand if the amniotic sac is superfluous, or as has been suggested, occasionally even a hindrance, the reverse should hold true and with ruptured membranes there should be a smaller percentage of prolonged labors. That this was actually the case was demonstrated by Schultze¹³ in 1929, who found that whereas the incidence of prolonged labor in 6,500 deliveries was 12.4 per cent, it was only 8.4 per cent in 600 dry labors; it was demonstrated again by Mason¹⁴ in 1933 who found 10 per cent of 1,000 consecutive labors extending over twenty-four hours, whereas only 2 per cent of the dry labors were prolonged. In this experiment, 6 per cent of the control "wet labor" cases were difficult and prolonged, but only 3 per cent of the dry labor cases.

Kreis¹⁵ has shown furthermore, in a study of nearly 3,000 cases, that at any given time there will be a larger percentage of women who have

completed the dilatation and delivery in the absence of membranes than with intact membranes. Figs. 1 and 2 show the ogive or cumulative distribution curves for primiparas and multiparas, respectively, in the 1,000 normal cases. It will be observed that when the membranes ruptured before the onset of labor, dilatation was completed faster than in the so-called normal cases, and as might be expected, the partially dry labor cases fell somewhere between the two. The dots on the charts represent Kreis' confirmatory percentages.

This group of "partially dry" labors lends itself to analysis of the rôle of the amniotic sac. If the hydrostatic wedge concept is correct, then the earlier the membranes rupture the longer the labor should be; that is, there should be a high *negative* correlation between the relative

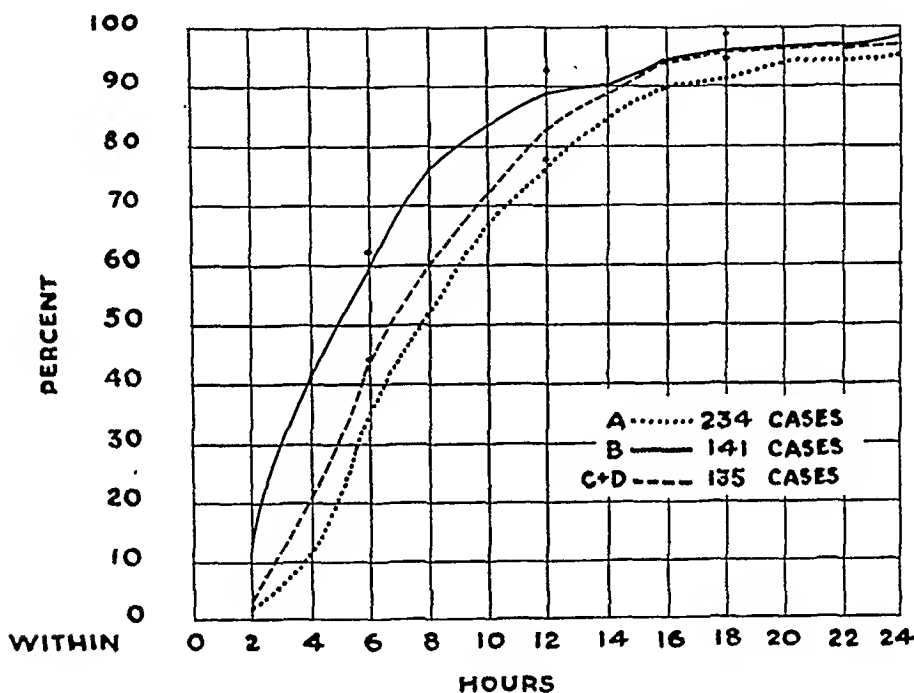


Fig. 2.—Ogive of labors completed, multiparas.

length of the "wet" portion of the labor and the total length of labor. The correlation may be worked out by plotting the total length of labor against the percentage of wet labor in each of the cases. Far from a high negative correlation in the 134 primiparas and the 130 multiparas so studied, there was a distinct and significant, even though small, *positive* correlation (0.20 ± 0.05 and 0.21 ± 0.05), that is, suggesting that the earlier the membranes ruptured the shorter the labor tended to be.

The simplest way of expressing the difference between so-called normal labor and dry labor and partially dry labor is by the averages of the lengths of labor. This is shown in Fig. 3. The control cases averaged 12.3 hours for primiparas; the partial dry group, 11.9 hours; and the dry labors, 10.3 hours. For multiparas the values were 8.5, 7.9, and 6.1 hours, respectively. The probable error of the mean in each case was

in the neighborhood of fifteen minutes.* These figures represent only labors terminating within twenty-four hours. Had the others been added the differences would have been even greater because of the larger number of prolonged labors in the "wet" group.

These results thus statistically confirm the conclusions of other writers on the subject, whose findings are presented in Fig. 4. Evidence that precocious rupture of the membranes leads to a higher percentage of prolonged labors or delays dilatation of the cervix and delivery, is conspicuous by its absence.

It will be remembered that when the hydrostatic wedge theory was first attacked, as early as the eighteenth century, preservation of the membranes was urged for other reasons, such as protection of the baby, and in later years the prevention of infection and cervical lacerations.

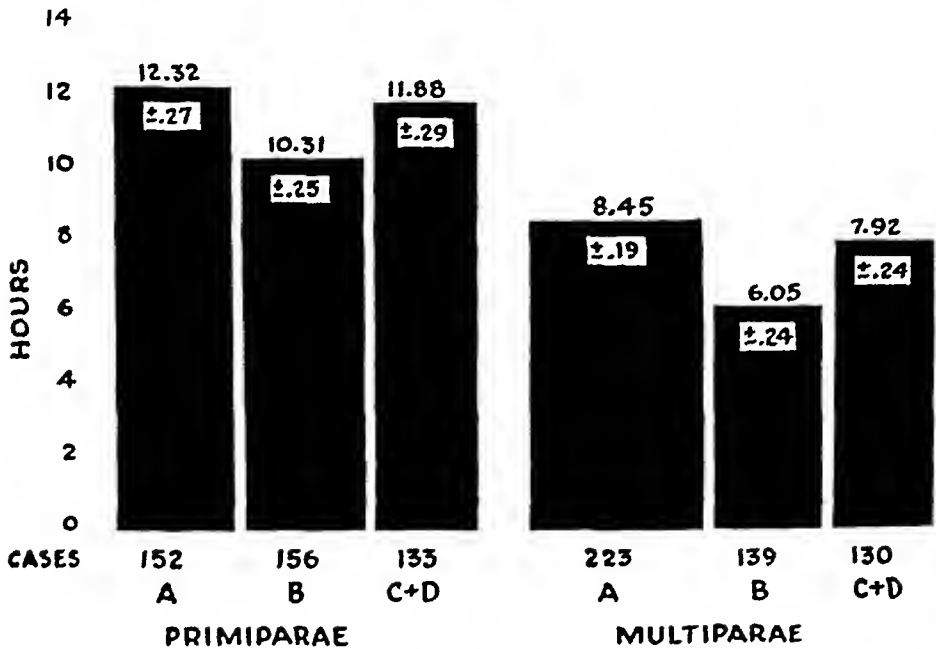


Fig. 3.—Average length of labor.

Again it must be pointed out that these are purely theoretical considerations. As W. D. Porter¹⁶ commented in 1923: "The dangers of dry labor are rather exaggerated . . . and the dangers mentioned do not develop as a rule." One of these dangers is the increased incidence of

*The values were derived by the Pearson Product-Moment Coefficient technic from the formula:

$$r = \frac{\Sigma x'y' - \frac{(\Sigma fdx)(\Sigma fdy)}{N}}{\sqrt{(\Sigma fd^2x - \frac{(\Sigma fdx)^2}{N})(\Sigma fd^2y - \frac{(\Sigma fdy)^2}{N})}} \pm \frac{0.6745(1-r^2)}{\sqrt{N}}$$

The P.E.M. was calculated from the formula: $0.6745 \times \frac{\sqrt{\Sigma fd^2}}{N}$ and the Reliability of the Difference from the formula: $\frac{\text{Diff}}{\sqrt{(\sigma M_1)^2 + (\sigma M_2)^2}}$. The values for the reliability of the difference between the control and the dry labor groups were 3.68 and 5.36 for primiparas and multiparas, respectively.

forceps application. In Table III are presented the figures in this series for indicated low, mid and high forceps, excluding the prophylactic use

TABLE III. INCIDENCE OF FORCEPS INTERVENTION

	LOW, MID, HIGH FORCEPS	MID AND HIGH FORCEPS
A	16.3%	6.2%
B	10.6%	3.5%
C, D	12.6%	4.2%

of outlet forceps. The highest incidence was found in the control group, the lowest in the dry labor group, with the partially dry labor cases again falling between. Since the indications for forceps are usually maternal exhaustion or fetal distress, and since the incidence varies as the length of labor in the three groups, it is suggested that the lowered incidence in the dry and partially dry labors is due to their being shorter with the concomitant saving of energy to the mother and trauma to the child.

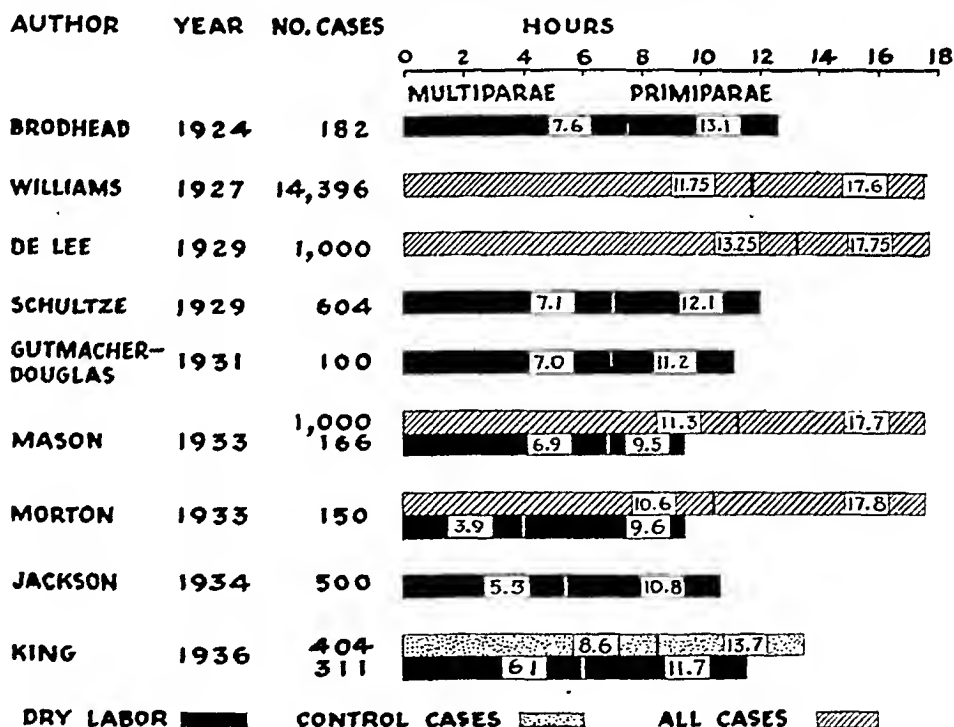


Fig. 4.—Average duration of labor.

Another of these dangers is that of infection. The morbidity in the 1,001 cases is given in Table IV. The standard used was that of the American College of Surgeons, a temperature of 100.4° F. on two successive days not including the first or later than the tenth day postpartum. It will be observed that the total morbidity was not appreciably raised and the morbidity from uterine causes was slightly lowered by premature rupture of the membranes. In this connection it is of some interest that Kreis first questioned the value of the membranes at the International Congress on Puerperal Fever at Strasbourg in 1922.¹⁸

From Denman's textbook³ in 1778 to Curtis'¹⁹ in 1933, the hydrostatic wedge has been considered gentle in its action on the maternal cervix. Norman Williams,²⁰ however, after a study of 150 cases in 1935, con-

TABLE IV. MORBIDITY (A. C. S.)

	TOTAL	CORRECTED
A	6.2%	2.7%
B	5.5%	2.6%
C, D	6.6%	1.0%
D	6.7%	1.1%

cluded that "the degree of dilatation at the time of rupture appears to bear a definite relationship to cervical injury . . . the tearing is found to be less when the membranes break before labor or early in labor." As shown in Table V this statement is to a certain extent confirmed in the 183 ward primiparas on whom postpartal data were available. From the limited number of cases no definite conclusions may be drawn, but it is apparent that intact membranes did not appreciably protect the cervix.

TABLE V. CERVICAL LACERATIONS
183 PRIMIPARAS

	NO. CASES	0*	0 AND FIRST DEGREE	SECOND DEGREE	THIRD DEGREE
A	55	20%	80%	20%	0
B	68	30%	87%	12%	1%
C, D	60	17%	84%	18%	0

*No lacerations.

A very old argument in favor of preserving the membranes is the protection of the child. This is hard to discuss because of the complexity of factors and an endless amount of theorizing in the literature. As there was no death in the 1,001 normal cases that might have been attributed to the delivery, all the neonatal deaths and the viable stillbirths in the 1,621 admissions are presented in Table VI. It will be noted that there is no evidence to suggest dry or partially dry labors without complication were harmful to the child.

Since the results of this experiment were so contrary to the usual teaching, it was felt advisable to compare them with the observations on dry labor of the past fifteen years. There are abstracted in Table VII the opinions of all authors who have actually recorded their findings. It will be noted that there is a preponderance of evidence that dry labor, whether spontaneous or induced, is either harmless or even favorable, and the length of labor is unanimously conceded to be no more prolonged as a result of rupture of the amniotic sac, thus casting grave doubts on the rôle that structure plays in cervical dilatation.

TABLE VI. VIABLE STILLBIRTHS AND TWENTY-FOUR-HOUR NEONATAL DEATHS
1,621 OBSTETRIC ADMISSIONS

		?	A	B	C, D
Dead before onset of labor		14			
Anencephaly, meningocele, etc., prematurity		4			
Intracranial hemorrhage		0			
True knot in cord			1		
Cord tight about neck:	Accidental hemorrhage	1			
	Difficult breech			2	
	Difficult forceps		2	1	1
Prolapsed Cord:	Transverse or breech presentation			1	1
	During difficult version or high forceps		1	1	
	After bagging			1	
	In hydramnios		1		
Undetermined	Breech			1	
	Vertex	1	1		
Total vertex		2	6	3	1
Total	(36)	18	2	6	7
				2	2

TABLE VII. SUMMARIZED OPINIONS ON DRY LABOR

AUTHOR	YEAR	NO. CASES	LENGTH LABOR	FORCEPS	MORBIDITY	FETAL DANGER	PROG- NOSIS
Dorman, Lyon ²¹	1921	270	Shorter	—	? Higher	? More	Same
Polak ¹⁷	1923	—	—	—	—	—	Poor
Brodhead ²²	1924	182	Shorter	Same	Same	Same	Same
Randall ²³	1925	88	Same	—	—	—	Same
Schultze ¹³	1929	604	Shorter	More	Higher	Less	Same
Norris ²⁴	1930	196	Shorter	More	Higher	Less	Poor
LaHaye ²⁷	1931	1250	Shorter	Fewer	Lower	Same	Good
Kreis ¹⁵	1931	—	—	—	—	—	Good
Fitzgibbon ²⁵	1931	220	Shorter	Same	Lower	Same	Good
Gutmacher ²⁶	1930	761	Shorter	Fewer	Lower	Same	Good
Slemmons ²⁸	1932	132	Shorter	—	Same	Same	Same
Mason ¹⁴	1933	166	Shorter	—	Lower	Less	Same
Morton ²⁹	1933	150	Shorter	—	Same	? Less	Same
van Rooy ³⁰	1933	—	—	More	—	—	Poor
Jackson ³¹	1934	500	Shorter	? Fewer	—	Same	Good
A. G. King ¹⁰	1934	300	Shorter	Fewer	Lower	Same	Good
E. L. King ³²	1934	—	—	—	—	—	Same
Woods ³³	1934	750	Same	? More	? Higher	Same	Same
Stern ³⁴	1934	85	Shorter	—	Lower	Less	Good
Holmes ³⁵	1934	90	Shorter	Same	Same	Same	Same
Rucker ³⁶	1935	716	Shorter	—	Lower	Same	Good
Krahulick ³⁷	1935	205	Shorter	—	—	—	Same
N. Williams ²⁰	1935	150	Shorter	—	Same	Same	Good
A. G. King	1936	597	Shorter	Fewer	Lower	Same	Good

SUMMARY

An investigation was made of 1,001 uncomplicated full-term parturitions occurring in 1,621 obstetric admissions. Of these, 40 per cent enjoyed intact membranes until complete dilatation and were used as controls. Thirty-one per cent spontaneously ruptured the membranes before the onset of regular pains at twenty-minute intervals, and were classed as dry labors. The remaining 29 per cent was made up of those whose membranes were intact only to a dilatation of from 4 to 7 cm., 11 per cent by spontaneous rupture and 18 per cent by deliberate rupture.

No light was thrown on the etiology of rupture of the membranes, although it occurred disproportionately more often in primiparas. Occipitoposterior position was not a factor.

The length of labor was studied from four points of view: There was a larger percentage of prolonged labors in the control group than in the dry and partially dry groups. The cumulative distribution curves of percentage completed labors at two-hour intervals, was most favorable for completely dry labors, least favorable for the "wet" labors, the partially dry labors falling between. In the partially dry labors there was a positive rather than a negative correlation between the length of the "wet" portion of the labor and the total length of labor. The statistically significant averages of the length of labor showed dry labor to be shorter than the controls by 2.0 (± 0.25) hours for primiparas and 2.4 (± 0.24) hours in multiparas.

Concerning the safety of labor in the absence of the membranes: The incidence of forceps intervention was 16.3 per cent in the control group, 10.6 per cent in the dry labor group, and 12.6 per cent in the partially dry labor group. The morbidity was essentially the same in all groups, i.e., 6.2 per cent in the controls, 5.5 per cent in the dry labor cases, and 6.7 per cent in the partially dry labors. There was a slightly lower incidence of cervical lacerations in the dry labor group than in the controls, with the partially dry labors falling between. The fetal mortality was unaffected by rupture of the membranes either spontaneously or deliberately.

The literature was exhaustively reviewed and reports in the last fifteen years amply confirm the above findings.

These results offer support to the explanation of cervical dilatation suggested by Dewees, that in labor the cervix is gradually retracted over the head by muscular action alone. On the other hand, that dilatation is accomplished by the hydrostatic wedge, a theory which has been disputed repeatedly since the eighteenth century, appears to be incompatible with the results of this experiment, inasmuch as the membranes proved to be unnecessary for a safe, easy, and short labor.

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3236 BURNET AVENUE

A SURVEY OF THE VAGINAL FLORA AT VARIOUS AGES, WITH SPECIAL REFERENCE TO THE DÖDERLEIN BACILLUS

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THE organism first discovered and described by Döderlein in 1892 has attracted the attention alike of bacteriologists, gynecologists, and obstetricians. Many students of bacteriology have been interested in this organism on account of its close relationship to the well-known intestinal type of lactobacillus, *L. acidophilus*. To the clinical group it is of particular interest because of the important rôle ascribed to it heretofore in the production of acidity of the vaginal tract. This acidity was and still is regarded by many as of prime importance in preventing infection of the genital organs, especially during pregnancy.

A number of investigators have made surveys of the prevalence of Döderlein's bacillus in the vaginas of individuals in various age groups. Much of their work has been done by the use of smear technics and cultural methods which appear to us to be inadequate for demonstrating the presence of the organism. In the work presented here we attempted to determine the frequency of occurrence of this bacillus in the vaginal tracts of children of various ages, pregnant and nonpregnant females, and in individuals infected with *N. gonorrhoeae*, using a culture medium which our experience has shown to be particularly favorable for the demonstration of members of the lactobacillus group. It was further desired to determine, if possible, from the data obtained, whether the Döderlein bacillus alone is responsible for the acid condition of the vagina, or whether the growth of the organism is merely a result of increase in H-ion concentration due to other factors. An

attempt was made also to determine what influence may be exerted by pathologic processes in the vaginal tract upon the presence or absence of the aciduric organism concerned here.

EXPERIMENTAL

In obtaining vaginal specimens for smear and culture, utmost precaution was taken to maintain as nearly aseptic conditions as possible. In infants and very young children the vulva was swabbed with tincture of green soap and dried with sterile towels. The labia were held apart with a gloved hand and a sterile swab inserted and drawn along the vaginal walls to absorb secretion; immediately, upon withdrawal, the swabs were immersed in a test tube containing 1 c.c. of sterile physiologic saline solution. A second swab was obtained in the same manner, for direct microscopic examination. In older children it was found impractical to use the green soap cleansing procedure because the groups, coming from charity camps, were too large to admit of this treatment. In these cases, with the labia spread as far apart as possible, it was relatively simple to insert the sterile swab through the opening of the hymen without contamination by contact with the vulva or anal region. Wherever contamination was at all suspected the swab was discarded. In pregnant and nonpregnant adults the specimens were obtained by inserting sterile vaginal specula and introducing the swabs directly into the vaginal vault. Adults with intact hymens were not included in this study.

All of the specimens were cultured within two or three hours after being taken. The swab was well rotated until the saline solution became cloudy. From one-half to three-fourths of this suspension was then plated in a medium having the following composition.

200 c.c. filtered tomato juice
5 gm. Difco peptone
10 gm. Difco peptonized milk
5 gm. Difco yeast extract
800 c.c. water
20 gm. Difco agar
pH adjusted to 7.5 sterilized at 180° C. for 8 minutes
Final pH near 6.6 to 6.7

The plates were incubated at 37° C. for forty-eight hours in an atmosphere containing 10 per cent carbon dioxide. They were then examined for the typical fuzzy colonies. Microscopic examination of a number of colonies, smooth and fuzzy, was always made in order to determine whether any of the smooth colonies contained the Döderlein organism. In no instance was this organism found to grow in any form other than that of the X or XY types. Reports of other observers to the effect that this organism may grow as a smooth colony may have been due to the use of media which particularly encourage this type of colony. The medium used in the work reported here has been found especially effective in accentuating the roughness of certain other members of the lactobacillus genus, namely *L. acidophilus* and *L. bifidus*. Further, unless pour plates are used, even on the medium described above, the organisms tend to grow in a smooth colony. It has always been observed by us that strains of the Döderlein bacillus which grow as the X or XY type of colony in a pour plate will be smooth in form when streaked on agar. Counts were made of the Döderlein colonies and those of all other bacteria appearing in the plate, and the results recorded in terms of percentage of Döderlein bacilli as compared with the total viable vaginal flora.

All of the smears were stained by Gram's method and the relative prevalence of aciduric rods, diphtheroids, gram-negative rods, and gram-positive cocci determined. A search was always made for gram-negative diplococci, and a hanging drop preparation examined for *Trichomonas vaginalis* in cases where a vaginal discharge was present.

RESULTS

A. *Children*.—The vaginal flora of 164 children was studied. The Döderlein bacillus was found to be present in 29 (17.7 per cent) of these individuals.

On further subdivision into the various age groups ranging from one to thirteen years, it was observed that of the children who were seven and one-half hours to six years of age (28 cases), 4 cases (14.3 per cent) showed the Döderlein bacillus. Of the children in the group aged seven years through twelve years (134 in number), 24 (17.9 per cent) harbored this vaginal organism. Only 2 individuals who were

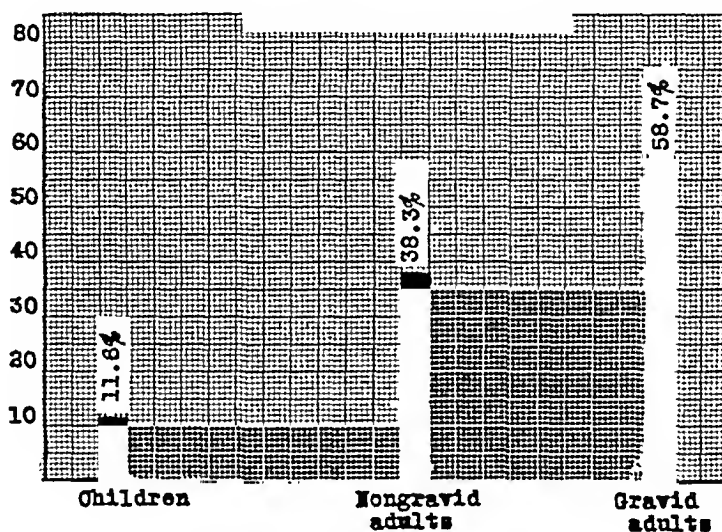


Chart 1.—Prevalence of the Döderlein bacillus in various age groups.

thirteen years old were studied, and of these only one had the Döderlein bacillus. Seven of the total number of cases studied had a vaginal discharge which could not be traced to gonorrheal or trichomonas infestation. Only 1 of these 7 patients harbored the aciduric bacillus.

B. *Nongravid Adults*.—Ninety-nine nongravid adult females were studied. Of these, 38 (38.3 per cent) showed the presence of the Döderlein bacillus, while 61 (61.7 per cent) had none. Further subdivision of this group into those complaining of vaginal disturbances (vaginal discharges or cervical lesions) and those having normal vaginal tracts, revealed that in the former group (45 in number), 17 (37.7 per cent) had Döderlein bacilli, and 28 (62.3 per cent) were apparently free from lactobacilli. In the latter group (54 in number), 21 (38.8 per cent) harbored the Döderlein bacillus, while 33 (61.2 per cent) did not. Of the group (45 in number) having vaginal disturbances, 10 of the 17 individuals who carried the Döderlein organism

suffered from a vaginal discharge, while 7 showed no discharge. Of those not harboring this vaginal bacillus (28 in number), 19 showed a discharge, and 9 did not.

C. Gravid Females.—A group of 97 pregnant women was studied. Of these, 57 (58.7 per cent) carried the Döderlein bacillus in the vaginal tract, while in 40 (41.3 per cent) the organism could not be demonstrated.

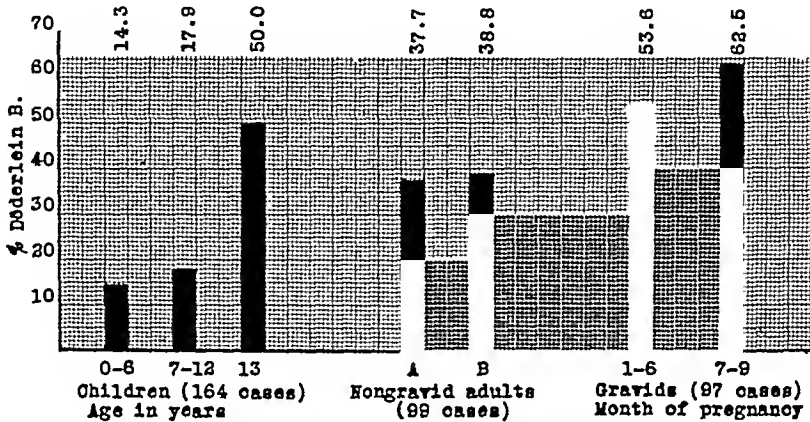


Chart 2.—In group of children, 7 showed vaginal discharge with no specific etiology; 1 showed Döderlein bacillus. A, Vaginal discharge or cervical lesion; B, normal vaginal tract. Group A, Döderlein bacillus present, 10 vaginal discharge and 7 no discharge; Döderlein bacillus absent, 19 vaginal discharge and 9 no discharge.

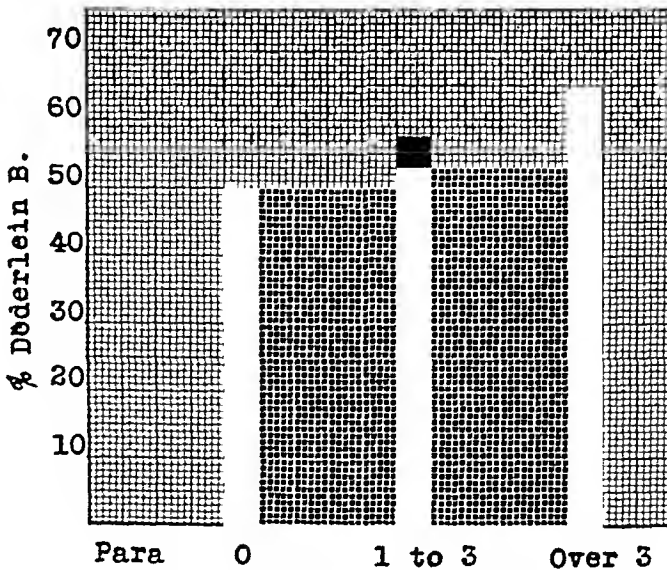


Chart 3.—Relation of Döderlein bacilli to number of pregnaneies.

When the total group was analyzed from the standpoint of the month of pregnancy in which the vaginal examination was made, it was found that in the cases which were gravid from one to six months (41 in number), 22 (53.6 per cent) showed Döderleins, while 19 (46.4 per cent) did not. Of those who were pregnant from seven to nine months (56 in number), 35 (62.5 per cent) had Döderlein bacilli, and 21 (37.5 per cent) did not.

Further subdivision of the group of gravid females, according to the number of children which they had borne, revealed that of those who had had no children (6 in number), 3 harbored Döderleins. Among women who had given birth to from 1 to 3 children (54 in number), 31 (57.4 per cent) showed this organism, while in 23 (42.6 per cent), it could not be found. Of 37 women who had more than 3 children (4 to 11), 24 (64.7 per cent) harbored Döderleins, while 13 (35.2 per cent) showed none.

Twelve individuals of the entire group of 97 studied had a vaginal discharge which was not due to gonococcus or trichomonas infection. In only 5 (41.6 per cent) of these was the presence of the Döderlein bacillus demonstrable.

D. Specific Infection of the Vagina.—Forty-two patients having specific vaginal infection were studied. Of these, 35 were found to harbor *N. gonorrhoeae*, while 7 were infected with *Trichomonas vaginalis*. It is of interest to note that none of these cases, the diagnosis of which was confirmed in every instance by stained smears, hanging drops and cultures, showed the Döderlein organism.

DISCUSSION

It should be noted in the results presented here that certain groupings of subjects have been made according to age in children, duration of pregnancy, and number of children in the pregnant groups. This grouping is purely arbitrary, and was decided upon for the purpose of working with significantly large groups.

Studies of the vaginal flora of 164 children revealed that 17.7 per cent harbored the Döderlein bacillus in their vaginal tracts. This figure is higher than that reported by Thomas⁵ in 1928, who, working with a smaller group, reported a 10 per cent occurrence of Döderleins. It is of interest to note that, with the exception of two cases (thirteen years of age), none of the children studied had menstruated. It is significant that of those who were in the age group of seven through twelve years (134 in number), only 17.9 per cent harbored Döderleins. None of these children had menstruated, but a large number of them showed beginning or marked secondary sexual characteristics. On the other hand, the children ranging in age from seven and one-half hours through six years, none of whom showed any of the sexual changes observed in the former group, exhibited almost the same prevalence of Döderlein bacilli (14.3 per cent). It is regrettable that only two children who had menstruated were available for study and that consequently no conclusions could be drawn from this group. However, in our study of nongravid adults the effect of menstruation was determined, since no nonmenstruating individual was studied.

An inspection of the results obtained in the examination of the vaginal flora of 99 nongravid adults reveals that 38.3 per cent harbored Döderlein's bacillus. There seemed to be no correlation between vaginal pathology and the presence or absence of the Döderlein organism, since in the group of women showing vaginal pathology, 37.7 per cent harbored Döderleins, while in the group revealing no pathology 38.8 per cent showed Döderleins.

The data obtained in the group of gravid females analyzed from the standpoint of duration of pregnancy show that a higher percentage of women pregnant from seven to nine months (62.5 per cent) harbored the Döderlein bacillus than did those of the group of individuals gravid from one to six months (53.6 per cent). Since the number of individuals in each of these groups is approximately the same, some significance may be attached to the difference noted. This will be discussed later. No correlation could be drawn between the parity of the individual and the presence or absence of the Döderlein organism. Twelve of the group of gravid individuals studied showed a vaginal discharge. The occurrence of Döderleins in this group was somewhat lower (41.6 per cent) than that of the group as a whole.

Many investigators have shown that the Döderlein organism is absent when gonorrheal infection is existent. Most of this work has been done by using the smear method for detection of the aciduric as well as the gram-negative diplococcic forms. In the present study these results have been confirmed by cultural examinations. Although the number of cases of trichomonas infection studied is quite small, it is interesting to note that the vaginal lactobacillus was not found in any of such cases. Further work along this line is desirable.

Attempts to correlate the findings in the smears with those obtained in culture were not successful in many instances. Very frequently organisms resembling the Döderlein bacillus were observed in the slide preparations, but could not be found by the culture method. The converse was also frequently true. This fact, we believe, is illustrative of the difficulty involved in attempting to study the prevalence of this organism by the use of smears only. It was noticed that in some of the slides where the aciduric organism preponderated, the diphtheroid and gram-negative forms were the first to disappear, and the group of gram-positive cocci the last. In other words, three types of flora could be observed, according to the smear picture. First, a pure or almost pure specimen of Döderlein's organism; second, the aciduric rods mixed with gram-positive cocci; and third, the aciduric rods, gram-positive cocci and diphtheroid cells. Gram-negative rods were seen only infrequently and then only in the third group. The three types of vaginal flora observed by us have been described previously by Crnickshank¹ (1930) and others.

The question of association of Döderlein's bacillus with increased H-ion concentration in the vagina has interested many observers. We believe that no evidence exists at the moment which is in full support of the theory that the organism alone causes the increased acidity. Analysis of the above data indicates that there is a gradual increase in prevalence of Döderlein's organism in children up to puberty, that the organism is to be found much more frequently in nongravid adults, and that it reaches its highest frequency level in the gravid adults in the last two or three months of pregnancy. It is a known fact that the vaginal H-ion concentration is lowest in children, higher in nongravid females, and highest in the pregnant females, especially in the last two or three months of gestation. It is also recognized that estrin is present in small quantities in prepubertal children, increases in amount as the menstrual function becomes established, and reaches its highest concentration during pregnancy and especially in the last two or three months. It has been shown by Hall and Lewis³ in monkeys (1936) and by Lewis and Weinstein⁴ in children, that the administration of estrin increases vaginal acidity, and that in some cases where Döderlein's bacillus was not present before administration of estrin, it was present after this treatment. Since the Döderlein organism is known to be favored by an acid medium, and the other members of the vaginal flora, such as the gram-negative rods, diphtheroids and gram-positive cocci are inhibited by a low pH, it seems probable that the presence of the vaginal bacillus is the result in many cases of the acid reaction brought about in the vagina by such factors as the natural or artificial introduction of estrin. The vaginal acidity does not seem to be due merely to the presence of the Döderlein organism, but it seems likely that the presence of the aciduric bacillus is facilitated by the increased acidity, which in turn is brought about by secretion of estrin.

CONCLUSIONS

1. A survey of the vaginal flora of 400 females of various ages revealed that 17.7 per cent of children, 38.3 per cent of nongravid females, and 58.7 per cent of pregnant women harbored Döderlein's bacillus.
2. There seemed to be only a slightly increased prevalence of the Döderlein organism with increase in age in the prepubertal group.
3. Döderlein's bacillus was found more frequently in the later than in the earlier months of pregnancy, and in the group of women who had borne 3 to 6 children, as contrasted with those who had given birth to 1 to 3 children.
4. Very little correlation could be drawn between vaginal pathology and the absence or presence of the aciduric vaginal bacillus, except in cases of gonococcus or trichomonas infection, in which Döderlein's organism was never demonstrated.

5. Three types of vaginal flora, as observed by other investigators, were noted in the direct microscopic studies.

6. Some evidence is presented in support of a theory that the presence of Döderlein's bacillus in the vagina is the result of the acidity induced by the secretion of estrin, and that the organism itself is not responsible for vaginal acidity.

The authors wish to express their appreciation to the Board of Governors, the supervisor and the clinical staff of the Bridgeport Dispensary for their permission to carry on this work and for their invaluable assistance in obtaining the material for study. Thanks are also due Drs. Fritz Meyer and Roland T. Wegher for their invaluable assistance in the work reported here.

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THE LE FORT COLPOCLEISIS*

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SINCE 1931, 38 cases of partial or complete genital prolapse in older women have been treated at the Chicago Lying-In Hospital by some modification of the Le Fort colpocleisis. This operation consisting of a medial obliteration of the vagina is seldom performed. The operation is applicable to a difficult group of cases, and the results have been so satisfactory that it would seem to be of value to report the cases with the method of treatment, since colpocleisis is seldom used and the literature is small compared with the great bulk written on the general subject of genital prolapse and its treatment.

The history of the surgical treatment of prolapse and the development of the operation may be of interest. The first attempts at surgical remedy consisted in an amputation of the protruding parts or a reduction of the size of the introitus to prevent their downward displacement. Frick of Hamburg (1832) sutured together the lower third of the labia majora. Credé, Baker-Brown, Dieffenbach, and Scanzoni denuded the tissues around the introitus and sutured the parts. Others removed portions of the vaginal walls and apposed the raw surfaces. All of these operations were done after a reduction of the prolapse. None of them were very successful.

As early as 1823 Gérardin of Metz adopted cauterization of the vaginal walls as treatment, and he first suggested that the anterior and posterior portions of the

*Presented before the Sixth Annual Fall Clinical Conference of the Oklahoma City Clinical Society, November 6, 1935.

Read at a meeting of the Chicago Gynecological Society, January 17, 1936.

vagina might be denuded at the introitus and the surfaces approximated by sutures. He did not perform the operation. It was first attempted by Neugebauer of Warsaw (1867). He denuded an area 3 by 6 cm. on the anterior and posterior walls near the introitus and sutured the anterior to the posterior wall at a somewhat higher level (3 cm.). His work was published in Polish journals (1867, 1870, 1871), but the method was not popularized until cases were reported by Léon Le Fort, Professor of Medicine, Paris, in 1876.

Le Fort knew nothing of the work of Neugebauer but followed the suggestion of Gérardin. He was led to use the colpocleisis as a result of his own work on congenital vaginal septum, the results of which he published in 1863. He observed that prolapse did not occur in cases of congenital septum of the vagina, and that, as a rule, normal sexual relations were possible and childbearing was not interfered with. Since treatment of prolapse was often necessary in women of childbearing age, a satisfactory operation must take these two factors into consideration.

Le Fort differed from his predecessors as to the cause of genital prolapse. He was of the opinion that in cases of genital prolapse, due to childbirth trauma or to congenitally poor tissue support, the hypertrophy and elongation of the cervix usually found, were secondary, not primary. He thought that the relaxation of the vaginal wall following childbirth, together with the usual rupture of the perineal floor, allowed a sinking downward of the anterior vaginal wall and the rectovaginal septum. The weight of the bladder upon the relaxed wall would result in a cystocele which would tend, in turn, to pull down after it the "next-lying vaginal wall." Traction would thus be put upon the cervix and in time lengthen both the supravaginal and infravaginal portions. The continuous, slight, downward traction would be responsible for the gradual prolapse of the corpus and its relaxed supports. He thought, therefore, that if it were possible to hold the vaginal walls in apposition and to prevent their sinking downward, it might be possible to prevent prolapse of the uterus.

His first patient, in 1876, was a twenty-nine-year-old woman, para iv, with a complete uterine prolapse, third-degree rectocele and cystocele. To the partial vaginal septum which he made, he added a perineal repair after the manner of Baker-Brown. The operation was successful. The following year the patient was delivered of a living eight-month fetus after a short, normal labor. The septum, of course, was incised. No recurrence of the original condition followed.

The technic of the operation as described by Le Fort is as follows:

"With the patient in the dorsal position and without attempting to replace the uterus, which was entirely outside the vulva, I made four incisions on the lower portion of the anterior wall of the vagina, circumscribing a strip of mucous membrane which, when removed, gave me a raw surface about 6 centimeters in length and 2 in breadth. Then, after raising and lifting the prolapsed uterus toward the abdomen, thus exposing the posterior surface of the tumor, I produced on this part a denuded surface similar to the one on the anterior wall. After doing this, I exposed the uterus sufficiently to permit joining the ends of the two raw surfaces which were closest to the uterus, and I applied sutures at three points on the transverse margin, uniting linearly the anterior and posterior walls of the vagina. I proceeded then to unite the lateral edges with a silver wire passed through corresponding points on the anterior and posterior margins of each side. A wire having been similarly placed at the same height on the opposite margin, the reduction of the uterus was increased by drawing together the apposed vaginal walls through a tightening of the two sutures. The reduction progressed step by step with the placing of the sutures, and when the two margins of the raw surfaces were united throughout, the reduction was complete." (Passage translated from original article by Léon Le Fort.)

In the years immediately following, numerous surgeons performed the operation, modifying the original technic. Eustache increased the width and depth of the vaginal septum, thus augmenting the stability of the uterine support and lessening the likelihood of recurrence of the prolapse through one of the lateral canals. This, however, interfered with coitus and reduced the applicability of the operation to women past the age of active sexual life. Duplay added a perineorrhaphy to the colpocleisis. After 1900 only occasional reports appeared in the literature until 1925. Since that time reports of small series of cases have been made by several operators (Brocq and Nora, Baer and Ries, Phaneuf, etc.). The history of the operation and the literature have been discussed at length because there is no such résumé in English and the material was found in old journals inaccessible to many practitioners.

In spite of the rarity of the performance of colpocleisis there would seem to be a place for such a procedure in a limited number of cases of prolapse. It is a relatively simple surgical procedure. It is admirably suited to elderly women and may be used when more extensive operations are contraindicated because of obesity, hypertension, chronic nephritis or evidence of myocardial weakness. In the cases reported here, 64 per cent had some condition contraindicating extensive operative procedure. It may be used with excellent results where other operative methods have failed. It can be carried out under local anesthesia or with a minimum of gas anesthesia or ethylene.

The prerequisites for the operation are as follows: The sexual life of the patient should no longer be of importance and the consent of the husband should be obtained. The cervix, corpus, and adnexa should be free from pathology. Schwabe thinks that all cases should be curetted prior to the operation and that phenol cauterization of the uterine cavity should be carried out. Erosions of the cervix and vaginitis should be eliminated by suitable treatment. The prolapse should be capable of reduction.

In the 38 cases presented here the ages of the patients vary from fifty-seven to seventy-three years (mean age = sixty-four years) and the duration of their complaint from one to forty-four years. One patient had never been pregnant; the rest had borne from 1 to 11 children. They were from four to twenty-eight years past the age of menopause. Nineteen (50 per cent) had had previous surgical treatment for the condition present. Eleven had worn various types of pessaries unsuccessfully.

The symptoms from which the patients suffered were chiefly urinary and pelvic. These included pollakiuria, dysuria, difficulty in urinating, retention of the urine with resulting cystitis and a sense of bladder

pressure. The discomfort of the prolapse and its interference with walking was a frequent complaint. Other symptoms were vaginal discharge and spotting, and in one case vulvitis.

On examination the pathology found was as follows: complete prolapse in 10 patients, complete prolapse with enterocele in 1, complete recurrent prolapse after hysterectomy in 4, partial prolapse with rectocele and cystocele in 18, and rectocele and cystocele alone in 5.

Surgical treatment was complicated by those conditions commonly found in elderly women—hypertension, obesity, albuminuria, and diabetes mellitus. The two cardiac patients were poor risks; another patient had been treated for pernicious anemia for some time.

Each case was given individual consideration in the choice of operation, and the colpocleisis was combined with other operative procedures as indicated by the pathology present. It was found that the addition of a perineorrhaphy added greatly to the results if a relaxed pelvic floor were present. A plication of the vesicovaginal fascia in cases with large cystocele also greatly improved the result of operation.

The operations performed were as follows:

Le Fort colpocleisis + plication of vesicovaginal fascia + perineorrhaphy	11 cases
Le Fort colpocleisis + perineorrhaphy	15 cases
Le Fort colpocleisis + repair of inguinal hernia	1 case
Le Fort colpocleisis + plication of vesicovaginal fascia + perineorrhaphy + repair of enterocele	1 case
Le Fort colpocleisis + vaginal hysterectomy	5 cases
Le Fort colpocleisis	5 cases

The operations were not all carried out by a single operator, but in general the technic consisted of three procedures:

1. Plication of the pubovesical fascia.
2. Le Fort colpocleisis.
3. Colpo-perineorrhaphy.

THE TECHNIC OF LE FORT COLPOCLEISIS

The patient is placed in the lithotomy position and the usual perineal and vaginal preparations, catheterization and draping completed. Either local anesthesia ($\frac{1}{2}$ of 1 per cent solution of novocaine) or light ethylene anesthesia is used. The cervix is grasped in the midline and drawn downward with a single-toothed tenaculum forceps.

The first step in the Le Fort colpocleisis is beginning the denudation of the anterior vaginal wall by a snowshoe-shaped incision of approximately 4 by 8 cm. The base of the incision is just above the bladder reflection. The vaginal flap is dissected free downward to the fascial layer and extended toward the urethra for a distance sufficient to expose the vesicovaginal fascia.

The bladder wall is exposed mesially close to the cervix and is pushed upward on the uterus. The fascia is split in the midline and is then sutured to the uterus underneath the bladder wall as in a cystocele operation.

The cervix is drawn forward and a similar flap of mucosa is freed posteriorly.

A transverse strip of vaginal mucosa about 2 cm. wide is thus left across each of the lips of the cervix. The margins of these anterior and posterior strips are sutured to one another with interrupted sutures, thus making a transverse channel below the level of the internal os. These interrupted sutures are inserted so that they enter and emerge on the vaginal surface and the knots, when tied, lie within the vaginal channels.

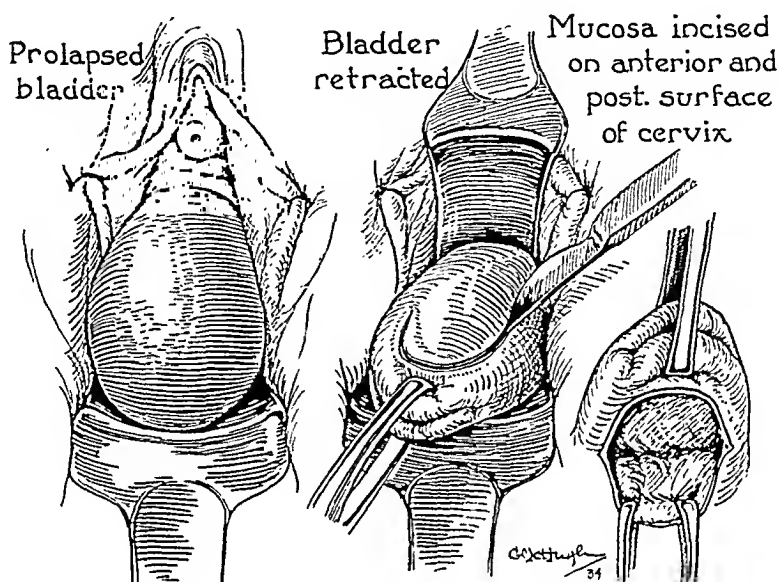


Fig. 1.

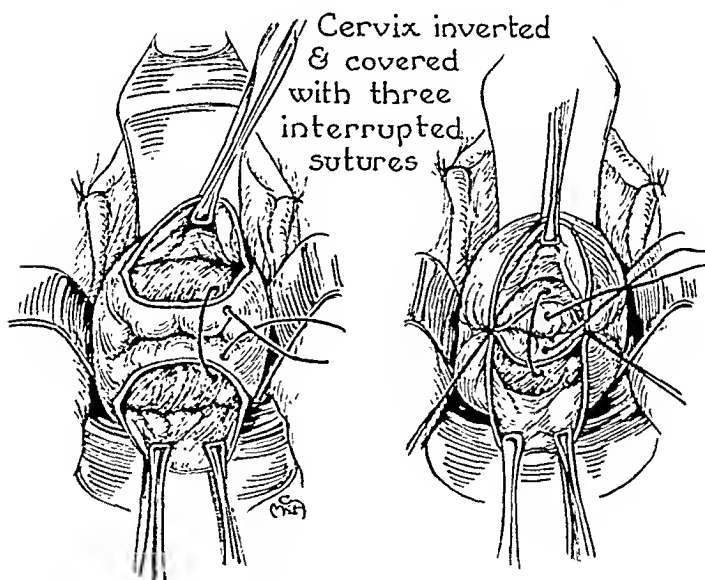


Fig. 2.

The lateral strips of vaginal mucosa are about 1.5 to 2 cm. wide, extending from the transverse cervical strip superiorly to a point about 1 to 1.5 cm. above the external urethral meatus and inferiorly to fuse with the perineorrhaphy incision.

The lateral margins of the vaginal mucosal flaps are sutured by interrupted sutures anteriorly and posteriorly. These sutures are inserted and tied with the knots inside the lateral channels as described above. As the margins are sutured

downward, the uterus recedes upward and gradually right and left channels about 0.5 cm. in diameter are formed which ultimately extend from the cervix downward to the introitus.

The operation is completed by a typical perineorrhaphy.

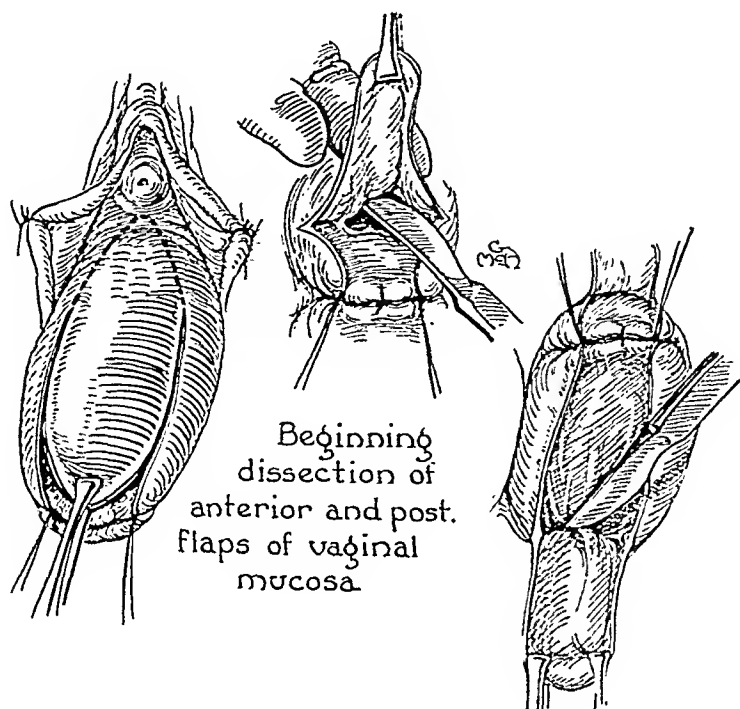


Fig. 3.

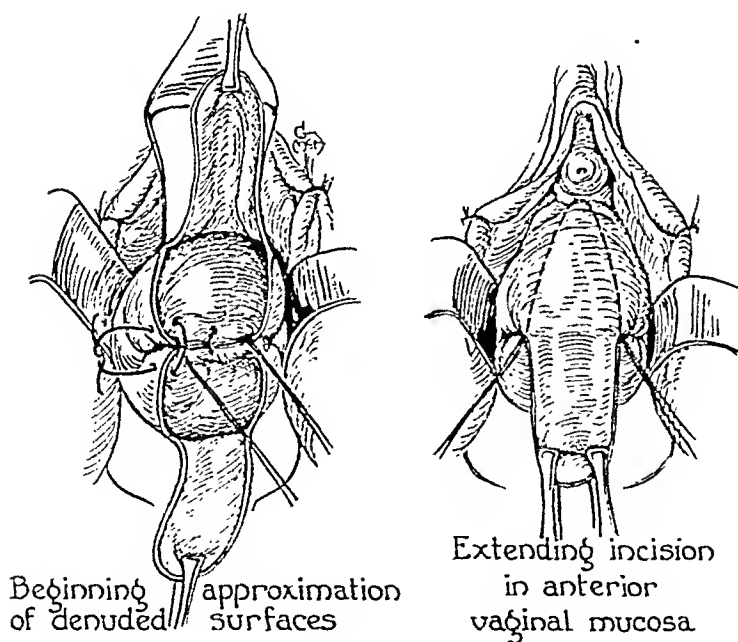


Fig. 4.

The lateral and transverse channels make an inverted U-shaped channel. The lateral channel of one side runs upward from the introitus to the cervix, passes across below the external os to connect with the lateral channel of the opposite side which extends downward to the introitus. The lateral channels can be easily demonstrated by the insertion of a uterine sound.

Convalescence.—The patient is usually awake before leaving the operating room. The light anesthesia required generally reduces postoperative nausea to a minimum. Patients are kept comfortable with small doses of morphine sulphate and placed on liquids and a light diet. They are encouraged to move about. Recovery is sur-

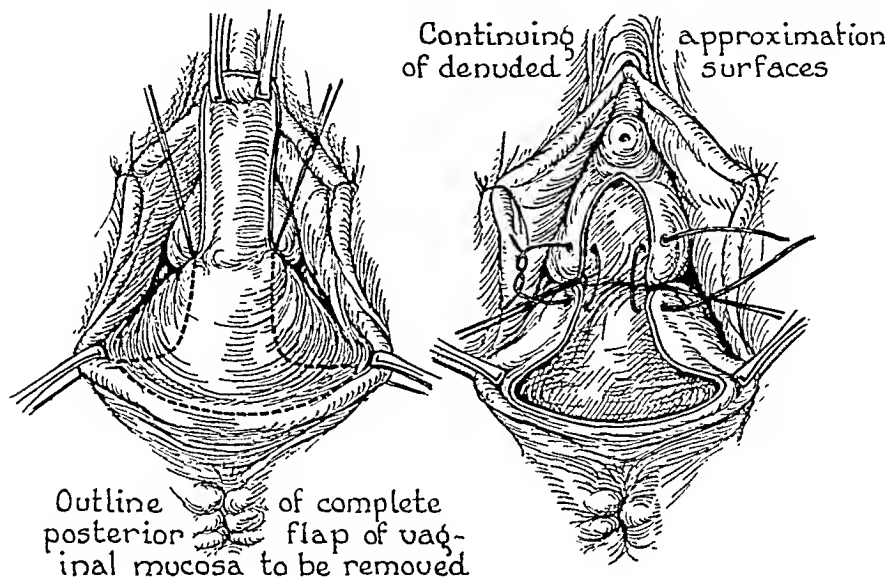


Fig. 5.

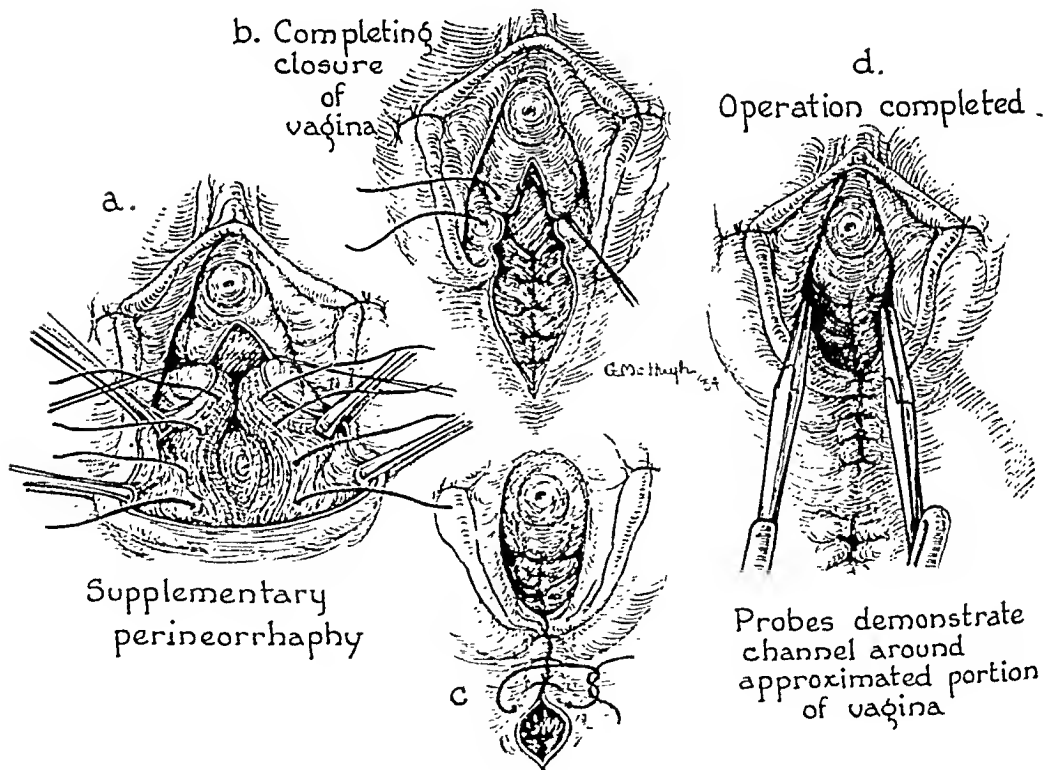


Fig. 6.

prisingly rapid. The patients in seven of the cases here reported had mild febrile reactions. Three developed a postoperative cystitis, and two had a slight discharge from the operative area. Three patients had prolonged hospital stays of seventeen and nineteen days. The remainder were up and about on the ninth and tenth post-

operative days and left the hospital on the twelfth or fourteenth postoperative day. There were two fatalities in the series, a mortality of 5.26 per cent. While the condition responsible for the first fatality was not directly connected with the operative procedure or a condition growing out of the event, it should be charged to the mortality since the patient died while in the hospital. The patient, aged fifty-eight years, had been considered a poor cardiac risk by the medical consultant; operation had been carried out under local infiltration anesthesia (novocaine $\frac{1}{2}$ per cent). On the eighth postoperative day the patient developed a coronary thrombosis which was followed by auricular fibrillation. A popliteal embolism occurred with resulting gangrene of the left leg; and on the thirty-ninth postoperative day the patient died from hypostatic pneumonia. The second fatality was due to pulmonary embolism in a patient who had slight postoperative fever. The embolus occurred after the patient had been allowed up on her thirteenth postoperative day.

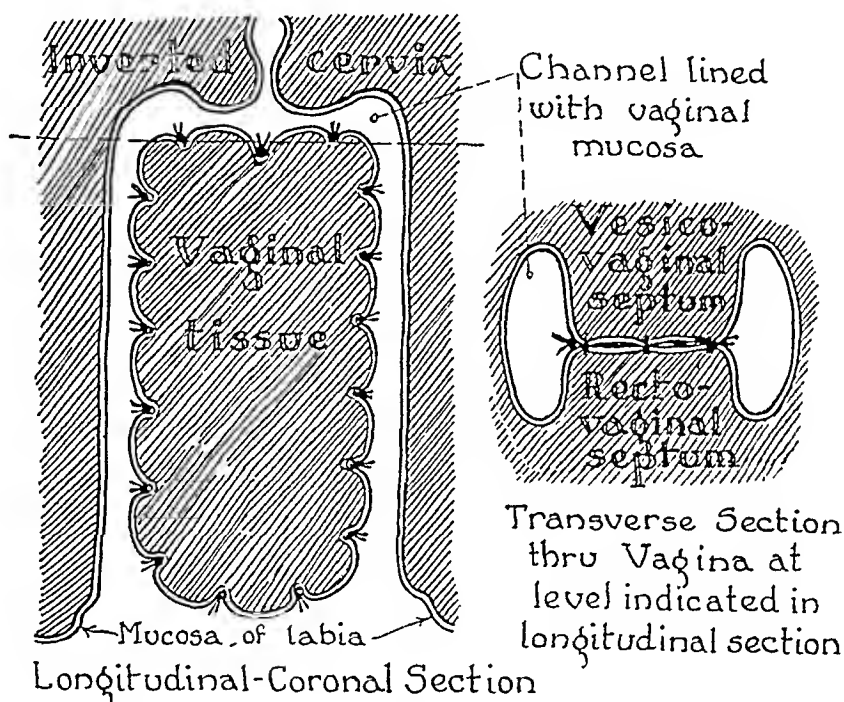


Fig. 7.

RESULTS

The results of the operation should not be finally appraised before the end of one year. In this series the follow-up of the survivors ranges from three months to over three years. To date there has been one recurrence. The uterus prolapsed through one of the lateral channels three months after operation. This was corrected by a secondary operation. In all of the other cases the functional results have thus far been excellent. In two of them the anatomic results were not entirely satisfactory. On inspection there was a very slight bulging anterior to the transverse line of suture. This slight cystocele might well have been due to failure to carry the denudation of the anterior vaginal wall low enough beneath the urethral meatus. In no case has there been failure of the surfaces to unite. Satisfactory final results were

thus obtained in 94.74 per cent of the cases in this series. This compares favorably with the results reported in the literature. In a total of 260 cases reported by various operators from 1867 to 1930, there was a satisfactory result in 86 per cent of the cases. It is of interest to note that the causes for recurrence of the prolapse have been almost universally the same: (1) Failure to make the lateral channel small enough to prevent recurrence of the prolapse through the side canal; and (2) failure of the sutures to hold, with resulting partial separation of approximated surfaces. Deaths have usually been due to thrombosis and cardiovascular disease.

There has been one major objection to the operation: the performance of colpocleisis precludes any further examination of the cervix. For this reason it is necessary that the cervix and the uterus should present no abnormality at the time of operation, and if any suspicious lesion is present, a vaginal hysterectomy should be done. However, the incidence of uterine carcinoma in women with atrophied uteri is indeed rare. We have found a report of only one case of carcinoma following colpocleisis.

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A married woman, aged twenty-six, who had never been pregnant began to suffer from backache and slight chilliness. She continued with her work. For days later her physician found a fever and lower abdominal tenderness. On the twenty-first day of the disease the patient was hospitalized with a temperature of 101.6° and pulse of 128. At operation a large left pyosalpinx and a smaller left pyosalpinx were drained. Cultures of the pus were made especially because the condition resembled tuberculosis. The convalescence was satisfactory. There was no evidence of diarrhea, constipation, nausea, etc.

By smear and cultural studies and agglutination and antigenic tests the organism was identified as Salmonella Newport. (This is a gram-negative bacillus and is a genus of the bacteriaceae.) Recovery of the organism from the blood, urine, and feces failed. The source of the infection could not be determined.

H. CLOSE HESSELTINE.

ACUTE NEPHRITIS AND PREGNANCY*

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COMPARATIVELY few reports of acute nephritis or nephrosis and pregnancy have been published. These conditions either are rare or are overlooked in the diagnosis. "Toxemia of pregnancy" is an inclusive term for all cases of edema, albuminuria, or hypertension in pregnancy. Disease of the vascular-renal system may be caused by the toxemia itself, or it may be pre-existent to the pregnancy, in which event it is usually aggravated. Many toxemia patients have symptoms and signs of acute nephritis or nephrosis, but they usually disappear rapidly after delivery. The abnormal findings, which we will describe, were found to persist in a small group of these patients.

Acute nephritis, hemorrhagic Bright's disease, or acute glomerulonephritis may be defined as the occurrence in a previously normal patient of proteinuria, cylindruria and hematuria. Edema, hypertension, and oliguria may also be present. A retention of the blood nitrogen and generalized convulsions may occur. Occasionally there are pathologic changes in the retinae. The disease usually appears during convalescence from some streptococcal disease, such as tonsillitis or scarlet fever. The onset is occasionally so insidious that its origin cannot be determined. It is self-limited and complete recovery may occur in a period of several months to a year and a half. If the abnormal urinary findings are still present at the end of two years, the disease is then considered a chronic glomerulonephritis.

Acute nephrosis, lipid nephrosis, degenerative Bright's disease or the nephrotic form of glomerulonephritis are the various terms used to describe cases without hypertension but with massive edema, marked proteinuria, slight, if any, cylindruria, and no hematuria. The characteristic findings in the blood are a decrease in the hemoglobin, a serum protein concentration of less than 5 per cent, an albumin: globulin ratio of 1 or less, a marked increase in cholesterol and total lipids, and little or no nitrogen retention. Doubly refractive lipid bodies, both free and in the casts, are found in the urine. The loss of protein in the urine tends to be constant and ranges from 5 to 50 gm. per day. If the previously described symptoms occur in a child or young adult, it may be a case of true nephrosis, as described by Leiter, but, in general,

*Read before the Chicago Gynecological Society, January 17, 1926.

it has been our experience that the majority of the cases seen by us are the atypical form of acute glomerulonephritis. This syndrome is often diagnosed "albuminuria of pregnancy."

The toxemias of pregnancy are characterized by vascular and renal pathology. The symptoms and signs may be present for a period of a few days or weeks or they may remain after delivery. The presence of albumin and casts indicates an abnormal condition of the kidneys and some investigators refer to such cases as the "nephrosis" or the "nephropathy of pregnancy." A patient with an acute toxemia of pregnancy, whether it is preeclampsia or eclampsia, may have blood in the urine on microscopic and macroscopic examination. In our experience, however, this abnormal increase in erythrocytes has been transient, disappearing within a few days. If the duration is longer and if there are other characteristic pathologic urinary findings, we believe that a diagnosis of acute nephritis is more likely to be correct. It seems obvious that if the same vascular spasm occurs in the kidney as is found in the vessels of the retinae and the brain, it may be the cause of albumin, casts and erythrocytes in the urine. These various conditions are described best by the following typical cases.

ILLUSTRATIVE CASES

Lipoid Nephrosis.—Patient 11, aged twenty-two years, was admitted to the hospital on Jan. 14, 1927, in her first pregnancy and at term on May 17, 1927. She had had an erysipelas of the face in May, 1926. Edema of the ankles was first noticed after she became pregnant. It gradually increased and dyspnea was noted during the past month. Marked pallor, general anasarca, a double hydrothorax, ascites, and a marked edema of the labia were noted on examination. The uterus was the size of an eighteen weeks' gestation. Ophthalmoscopic examination showed edema of the retina and disk of the right eye, and slight edema of the left retina. The blood Wassermann was negative. An x-ray diagnosis of bilateral maxillary sinusitis was made. The patient was discharged on Feb. 7, 1927. She was readmitted on February 27 and was delivered of a macerated fetus. After the delivery she became even more edematous and there was a marked oliguria. On March 18, examination of the eyes showed an optic atrophy of the right eye and questionable involvement of the left. She was discharged on March 30. On June 6, 1927, she again returned and was found to be eight weeks pregnant. An abdominal hysterotomy and sterilization were performed on June 18, 1927. The patient stated that she had repeatedly observed swelling of the extremities following the ingestion of fat, even in minimal amounts, while she was still seated at the table.

During hospitalization the patient was on a chloride-poor diet, which consisted of 150 gm. of protein, 150 gm. of fat, and 300 gm. of carbohydrate. The diet yielded 3,200 calories, but she never consumed over 2,500 calories and usually much less. A sufficient amount of protein was never consumed. The nitrogen intake over a sixty-five-day period ranged from 5 to 21 gm., with an average of 7.4 gm. per day. The average total nitrogen in the urine was 7.9 gm. per day. The protein in the urine ranged from 7 to 22 gm. per day. In a period of nineteen days she lost 14 kg. in weight. She did not cooperate well after delivery and was seen irregularly. From 1930 on there was little or no edema, but her blood pressure had started to increase. In 1934 there was a very definite anemia, for which she was given a blood transfusion. The patient died of uremia in December, 1934. No autopsy was

performed. The clinical course and termination, however, indicate that what at first appeared to be a lipoid nephrosis was, in all probability, a nephrotic type of glomerulonephritis (see Table I).

Acute Glomerulonephritis.—Patient 1, aged twenty years, was admitted to the hospital on Sept. 12, 1933, in her first pregnancy, and approximately seventeen weeks pregnant. She had always been well until the onset of edema of her feet and lower legs one month previously. At this time there was urinary frequency, burning on urination, nocturia, and the urine was dark. Examination showed a two-plus edema extending up to the knee and a blood pressure of 154/90. The patient was treated for one month, with no improvement and possibly some increase in the severity of the process, as indicated by the decrease in the clearance, the anemia, etc. A therapeutic abortion was performed on October 13. The subsequent course was that of a chronic glomerulonephritis. There was a persistent albuminuria, varying from 5 to 12 gm. per day, with casts and a slightly increased number of erythrocytes, according to the Addis technic. The patient has been on a salt-

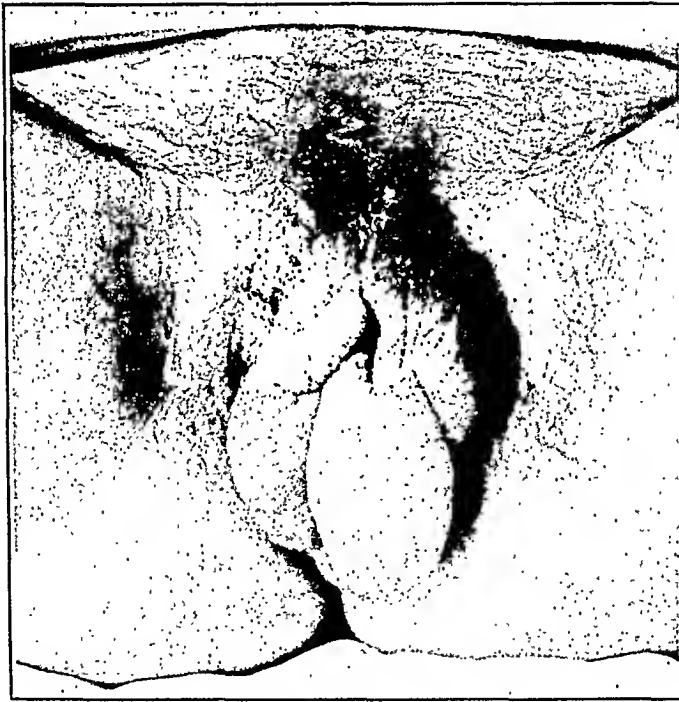


Fig. 1.—Patient 5. Nephrotic glomerulonephritis. Note marked swelling of vulva, which was present for one week.

poor general diet since her discharge from the hospital but the edema still persists. Because of the lowered serum protein and especially the lowered oncotic pressure of the serum she has been on a high protein diet for the past year. Her last blood pressure was 155/110. There is still a two-plus edema. On Dec. 17, 1935, she returned again and was found to be pregnant. A therapeutic abortion was performed on Jan. 14, 1936 (see Table II).

Nephrotic Glomerulonephritis.—Patient 5, aged twenty years, was admitted to the hospital on May 8, 1935, in her first pregnancy. She was approximately sixteen weeks pregnant. In January she had an unusually severe respiratory infection with a sore throat, after which she complained of nocturia and marked vomiting during February. The vulva had been swollen for one week. The swelling decreased slowly (Fig. 1). There was no other edema at any time. Ophthalmoscopic examinations on May 14, 21, and June 5 were normal. A vaginal hysterotomy was performed on June 4, 1935. On June 19, a diagnosis of bilateral retinopathy was made.

TABLE I. No. 11, Lipoid Nephrosis

DATE	WT. KILO.	B.P.	EDEMA	HB. GM. %	HEM. %	SERUM PROTEIN	A:G RATIO	N.P.N. MG. %	CHOLES- TEROL		URINE	
									ALB.	CASTS	R.B.C.	
1/14/27	67.3	154/ 90	+++		29	3.2	1.0	30	560	2.0	0	0
a. 3/30/27	51.0	120/ 70	+	11.0	35	3.7		28	510	0.4	+	+
b. 6/15/27	55.7	150/ 75	++	10.3	31	3.4		37	466	0.4	0	0
2/ 7/28			++	13.5	34	3.5		33	500	0.4	0	0
3/ 2/32	48.0		0	12.3	36	5.6	1.3	89	390	0.7		
c. 10/26/34		190/120		5.8	14	5.4	1.1	200	256	0.6		

a, Spontaneous abortion on 2/27. b, Hysterotomy and sterilization on 6/18. c, Died in December, 1934.

TABLE II. No. 1, Acute Glomerulonephritis

DATE	WT. KILO.	B.P.	EDEMA	HB. GM. %	HEM. %	SERUM PROTEIN GM. %	A:G RATIO	N.P.N. MG. %	URINE				STAND. CLEAR. %	
									ALB.	CASTS	R.B.C.	U/B		
9/11/33	48.8	154/90	+	11.0	30	5.3	1.3	27	15	++	++	++	29	57
a. 10/10/33	49.1	160/100	+	9.7	28	5.7		32	17	++	++	++	24	25
10/23/33	51.0	130/90	+	7.7	23	5.8		22	10	++	+	+	24	40
11/21/33	49.2	145/100	+		31	5.9		25	14	++	+	+	12	38
b. 10/9/34	51.0	114/70	+	12.4	38	5.4	1.1	29	15	0.5%	+	?	33	100
11/6/35	51.7	170/115	++	13.2	39	5.9	1.7	27	14				15	57
12/17/35	51.2	160/110	++			6.6		29	11	0.3%	0	0		
c. 1/13/36	52.0	155/100	++	11.5	35	5.1	1.6	26	15	0.4	++		31	52
1/28/36	48.5	140/100	+	13.4	43	5.8	1.5	43						

a, Therapeutic abortion. b, Double protein intake. c, Therapeutic abortion. 1/28/36 = cholesterol—490 mg. %.

TABLE III. No. 6, NEPHROTIC FORM OF GLOMERULONEPHRITIS

DATE	WT. KILO.	B.P.	EDEMA	H.B. GM. %	HEM. %	SERUM PROTEIN GM. %	A:G RATIO	N.P.N. MG. %	UREA %	URINE			
										ALB.	CASTS	R.B.C.	U/B
5/ 8/35	58.5	140/ 68	+	9.3	23	4.6		46	31	+++	++	+	21
5/20/35	62.7	130/ 80	+	6.3	22	4.4	1.6	54	34	+++	++		22
6/ 3/35	64.0	130/ 80	+	7.7	23	4.8		57	52	1.0	++	+	15
6/ 7/35		160/ 90	+	10.0	28	4.9		63	41	1.7%	++	+	12
6/27/35	60.3	185/105	+	12.2	36					+++	++	+	
6/30/35		180/110	++			4.1	1.8	49	24	+++	+++	+	29
12/23/35	55.1	180/100	++			4.9	0.7	48	28	2.0%	+++	0	14

a, Therapeutic abortion. b, Discharge. c, Readmission with convulsions.

Three small blood transfusions were given because of an anemia. She was discharged from the hospital on June 27. Following her discharge she remained in bed, and on June 30 she complained of a severe headache followed by vomiting. She soon became stuporous and had a convulsion with coma. On readmission to the hospital she was drowsy, edematous, and had a blood pressure of 180/110. A few minutes afterward she had an acute generalized convulsion. She was transferred to the medical service and was discharged by them on July 14, 1935. Contraceptive instructions were given to the patient. On Dec. 16, 1935, her blood pressure was 180/100. During the first admission to the hospital the determined oncotic pressure on two occasions was 11.4 (calculated 15.5) and 17.2 cm. (calculated 19.0) of water. She would not eat all of the high protein diet. As much as 21 gm. of protein was excreted in the urine per twenty-four hours. This case was diagnosed as glomerulonephritis of the nephrotic type (see Table III).

Recurrent Acute Glomerulonephritis.—Patient 6, aged nineteen years, was seen on the surgical service on Feb. 22, 1933, because of nausea and vomiting. Her blood pressure then was 120/94. The urine contained albumin two-plus, hyaline casts, and the nonprotein nitrogen was 40 mg. per cent. A urea clearance at this time showed 52 per cent of normal. The renal symptoms were thought to be due to the dehydration. On April 16, 1935, when the patient was six weeks pregnant, she was seen in the prenatal clinic. At this time the blood pressure was 140/90 and the urine contained albumin two-plus, with hyaline casts. A therapeutic abortion was contemplated but the patient developed German measles, and by the time she recovered, pregnancy was well advanced. The albuminuria persisted and the blood pressure, despite treatment, gradually increased to a peak of 220/150 on Oct. 18, 1935. The patient gained 13 kg. in weight, and although she was not at term until November 6, an elective cesarean section with sterilization was performed. The urine at this time contained a large number of erythrocytes which persisted until the last examination on Dec. 6, 1935. At this time her blood pressure was still 200/140. It is possible that this patient had an essential hypertension, with a superimposed acute nephritis at term. However, in view of the history, symptoms, and signs at the time of delivery and their persistence over a period of six weeks, a more likely diagnosis would be a chronic glomerulonephritis with an exacerbation caused by the pregnancy (see Table IV).

The four patients whom we have described so far all have had varying degrees of hypertension, proteinuria, and edema. The last patient developed a hypertension early in pregnancy, without any other symptoms, which persisted after delivery. A résumé of the history is included for comparison.

Essential Hypertension.—Patient 91383, aged twenty-three years, was first seen on Oct. 5, 1933, at which time her blood pressure was 110/80 and the urinalysis was negative. She was approximately nine weeks pregnant. On Oct. 28, 1933, her blood pressure was 170/105 and remained high. On Feb. 25, 1934, she had a spontaneous delivery of a living infant weighing 1,100 gm., and a partial abruptio placentae. On June 5, 1934, her blood pressure was still 220/150, and on September 4 an abdominal hysterotomy and sterilization were performed for a six weeks' gestation. On September 28 the blood pressure was 240/126. Ophthalmoscopic examination on February 28 was negative, but on September 3 there was a definite neuroretinitis. The urea clearance on repeated examinations has been between 50 and 60 per cent of normal, and the urine has never contained albumin, casts, or blood. On July 12, 1935, the patient's family physician stated that she was having a persistent epistaxis. This patient undoubtedly has a malignant hypertension which has been accelerated by the pregnancy.

Acute Glomerulonephritis With Death.—Patient 55019, aged twenty-two years, gravida v, para iv, was admitted on Feb. 15, 1932, approximately twelve weeks pregnant. She noticed edema of her legs for ten days and of her hands for one day,

TABLE IV. No. 6, RECURRENT ACUTE GLOMERULONEPHRITIS

DATE	WT. Kilo.	B.P.	HB. gm. %	HEM. %	SERUM PROTEIN gm. %	A:G RATIO	N.P.N. mg. %	UREA %	URINE			
									ALB.	CASTS	R.B.C.	U/B
4/25/35	50.8	140/90		35			25	11	++	++	0	45
7/29/35	57.5	150/100	11.9	34			26	13	0.1	+	0	59
9/26/35	63.0	168/123	12.9	33	6.8	2.0	27	12	0.3	++	+	35
10/21/35	63.2	190/150	12.6	40	7.7	1.3	27	14	0.6	+++	++	35
11/25/35	51.8	190/150	15.7	45	7.9	2.0	38	15	0.2%	+++	+	28
12/ 6/35	52.7	200/140							+++	++	+	

a, Cesarean section and sterilization. b, Hypertensive encephalopathy.

TABLE V

NUMBER	AGE	GRAVIDA	MINIMAL WEIGHT (KILO.)	WEIGHT LOSS (KILO.)	ETIOLOGY AND DURATION OF SYMPTOMS	DURATION OF PREGNANCY WEEKS	TERMINATION OF PREGNANCY	BLOOD PRESSURE	EDEMA	URINE			HEMOGLOBIN G.M. %	SERUM PROTEIN G.M. %	CHOLESTEROL MG. %	N.P.N. MG. %
										ALBUMIN	CASTS	R.B.C.				
1	20	i	50	2	Edema for 5 weeks	17	T. A.	140/90	++	+++	+	+	11.0	5.3	270	27
2	18	i	46	11	Hematuria for 3 months	28	Spon. term	152/100	++	+++	+	+	12.2	6.8	464	27
3	22	v	58		Diphtheria and nephritis 6 weeks	13	Abortion	160/120	++	+++	+	+	5.5	5.7	293	53
4	16	i	40	16	Edema for 3 weeks	23	Abortion	200/150	++	1.8%	+	0	12.6	4.2	*526	31
5	20	i	52	12	Edema of labia Cold, 4 mo. previous Edema of labia	16	T. A.	180/110	++	+++	+	+	5.5	4.2	298	63
6	19	i	51	13	Albumin and hypertension 6 months	10	C. S. + S.	200/140	++	+++	+	+	15.2	6.8		27
7	38	viii	69	6	Hypertension since 1931	18	T. A.	260/135	++	0.7%	+	+	13.8	6.1		35
8	26	iv	43		Acute nephritis 6 months previous	14	T. A. + S.	125/70	+	+++	+	+	6.4	6.4		30
9	20	i	43	2	Nephritis 3 years Edema of eyes 1 year	17	T. A. + S.	205/110	0	+	+	+	11.0	6.9		41
10	17	i	59	19	Headache and edema of labia 1 month	38	Spon. term	190/150	+++	2.5%	+	+				40
11	22	i	48	19	Erysipelas 1 year Edema for 2 months Edema of labia	18 +10	Abortion T. A. + S.	154/90	+++	2.0	+	0	9.0	3.2	560	30
12	16	i	50		Edema 1 month	37	Spon. term	170/125	++	1.2	0	0	11.0	5.4	511	30

T.A., Therapeutic abortion. S., Sterilization. Spon. Term., Spontaneous labor at term. C.S., Cesarean section.

*Total lipid = 2018 Mg. %.

†second pregnancy.

hematuria for six weeks, and vomiting for three months. In January she had had diphtheria and the urine was colored at that time. The hemoglobin estimation was 5.5 gm. per cent, serum protein 5.7 gm. per cent, nonprotein nitrogen 53 mg. per cent, and blood urea nitrogen 32 mg. per cent. A diagnosis of acute glomerulonephritis was made. Several blood transfusions were given. On February 24 marked dyspnea and coma were present, and on February 25 she aborted. Death occurred on March 1. The autopsy findings were: acute glomerulonephritis, extensive thrombophlebitis of both ovarian and popliteal veins, infarcts of both lungs, and embolism of the pulmonary arteries. The nephritis, which was the cause of the anemia, was undoubtedly the primary cause of the extensive thrombophlebitis.

Pertinent data from the patients in this series are listed in Table V. These cases have been collected over a period of twelve years, during which time approximately 22,000 patients have been delivered. All of the patients, with but one exception, were young. Edema was the complaint of 6 on admission. We were able to determine a possible etiology in only 4 of the cases. In 9 of the patients the disease was noted before the twentieth week of pregnancy; 4 patients went to term, but therapeutic abortion was prevented by other factors in one case. There were 3 spontaneous abortions and 6 therapeutic abortions. Four patients were sterilized. The increased blood pressure in the patients with lipoid nephrosis was thought to be caused by the pregnancy because of the rapid decrease after delivery, although the other symptoms persisted. The serum protein concentration was unusually low in the patients with nephrosis. Hypercholesterolemia was present in 4 out of 7 patients, anemia was marked in 3, and a nitrogen retention was present in 2.

The edema was usually general, and in the patients with nephrosis there was an associated hydrothorax and ascites. Marked edema of the labia was present in 4 out of 5 of these patients.

The excretion in the urine of large amounts of protein over a long period of time is characteristic of the nephrotic cases. The high concentration of 1.8 to 2.5 per cent for the twenty-four-hour period is striking.

Erythrocytes and various types of casts were present on repeated examination of the urine in those patients with a plus mark in the proper column.

DISCUSSION

Normal pregnancy is characterized by a tendency toward edema, slight albuminuria and a retarded elimination of water. Elden and Cooney, in a small series of normal pregnant women, have noted that the Addis count is higher than in normal nonpregnant individuals. Dieckmann and Wegner and other observers have described the relative anemia, decrease in serum protein concentration, hypercholesterolemia, and lipemia seen in normal pregnancy. Epstein has mentioned pregnancy as a cause of lipoid nephrosis, but in a personal communication in 1927, he was unable to point out a definite relationship. Several cases of nephrosis have been reported in which the onset was dated from a

pregnancy. The tendency toward edema, albuminuria, faulty water elimination, and abnormal fat metabolism observed in normal pregnancy is characteristic of nephrosis. It would seem reasonable that the symptoms of a nephritis or a nephrosis, if it developed during pregnancy, would be made worse because of the changes incidental to the latter condition. In our cases this was certainly true.

Numerous tests have been devised for determining the function of the kidneys. These have been reviewed in a previous article, where it was pointed out that pregnancy per se causes very definite alterations in these various tests. The urea clearance test in pregnancy has a prognostic or diagnostic value only if there is a constant clearance of less than 50 per cent of the normal, with a urine volume of 1 c.c. or more per minute, or if there is a persistent decrease, as in the first case described. The presence of protein in the urine is only suggestive of nephritis, and may be caused by cystitis, pyelitis, or a nephrosclerosis. Similarly, the presence of hyaline or granular casts is not indicative of nephritis. They may or may not be present in proved cases of chronic nephritis. Erythrocytes in the urine may be due to renal stone, tuberculosis, tumor, or to hydronephrosis with intermittent capillary ruptures. Hematuria may also occur if there is a marked increase or decrease of the blood pressure, as seen not infrequently in the toxemias of pregnancy. However, in these patients it is present for a few hours or a day at the maximum. What are the criteria necessary for a diagnosis of acute nephritis? These have been mentioned in the definition given for this condition, but we wish to emphasize the persistence of the erythrocytes in the urine for a period of a week or longer as evidence of acute glomerulonephritis. Likewise, the persistence of edema and albuminuria, despite the delivery, is indicative of a nephrosis.

In a period of four years, 398 microscopic examinations of catheterized specimens of urine were made by the author in 450 clearances; 100 patients with abnormal urine findings were found. A modification of the Addis technic was used and the number of erythrocytes was increased and found over a period of one week or longer in the urine specimens of 41 patients. Eight of these, Nos. 1, 2, 3, 5, 6, 7, 8 and 9, an incidence of 0.05 per cent, were diagnosed as "acute or recurrent acute glomerulonephritis." In the remainder, the transient hematuria was thought to be due to a "pregnancy toxemia." Casts were found in the urine of 48 patients.

Questionnaires were sent to 12 physicians in charge of large obstetric services or of large groups of patients with nephritis. Six replies were received, but only 3 contained data which could be used.

Mussey and coworkers of the Mayo Clinic have been able to group their toxemias of pregnancy according to the classification of nephritis used by Volhard and Fahr. In a recent communication Mussey reemphasized their beliefs and stated that "practically all of the 'acute nephritis' accompanying pregnancy is a part of the

toxemie picture and is merely a local manifestation of this condition." They observed one patient who, as a child, had an acute glomerulonephritis, recovered, and later in life went through pregnancy with no evidence of nephritis or toxemia.

Wegner of the Washington University has kindly permitted the use of the following data which he is preparing for an article on lipid nephrosis. During the period in which 10,596 deliveries occurred, there were 6 patients with acute glomerulonephritis and 3 with lipid nephrosis, an incidence of 0.056 and 0.028 per cent, respectively. In all of the cases the renal condition seemed to be exacerbated as pregnancy advanced. There was 1 therapeutic abortion, 5 premature labors (3 induced and 2 spontaneous), and 3 deliveries at term. He had 1 patient who went through an uneventful pregnancy after an acute glomerulonephritis. Two patients who had had acute nephritis died, and of those with nephrosis, 1 died, thus giving a mortality rate of 33.3 per cent for each condition.

Eastman, of the Johns Hopkins University Hospital, stated that during a ten-year period they had 16,150 admissions to the hospital, 10,965 deliveries, and 641 cases of chronic nephritis. In the nephritic group there were 2 cases of acute nephritis during pregnancy and 3 cases of questionable lipid nephrosis. The incidence is 0.018 and 0.027 per cent, respectively.

Barach and Boyd treated a twenty-year-old patient with nephrosis, using various procedures, and finally reported that after 295 gm. of gum acacia had been injected intravenously over a period of four weeks, there was a clinical cure. Two years after the injection of the acacia the patient passed through an uneventful pregnancy and puerperium and was in an excellent condition six months after the delivery.

Addis, in his monograph on nephritis, lists 2 patients out of a total of 72 in whom a "pregnancy toxemia" may have been the cause of the arteriosclerotic Bright's disease which caused their deaths, twenty-two and seven years, respectively, after the pregnancy. In a third case, pregnancy may have been the cause of a hemorrhagic Bright's disease which he studied during the terminal stage. A fourth patient, who had a terminal hemorrhagic Bright's disease, became pregnant twice but was always aborted.

Murphy and coworkers, in a recent analysis of 94 cases of diffuse glomerulonephritis, stated that in 16 cases (17 per cent) pregnancy was the only etiologic factor that they could find. Six of these patients recovered, 7 became chronic, and 3 died. They stated that "our autopsy studies in connection with these cases lead us to believe that acute diffuse glomerular nephritis due to eclampsia is practically the same as that due to other causes." They also stated that "the acute phase of glomerular nephritis may be so mild that it passes unrecognized, and no indication of renal damage is observed until the disease has progressed into the chronic stage, when renal insufficiency sets in."

Volhard lists pregnancy as the cause of the acute glomerulonephritis in 4 cases, and Lichtwitz in 2, according to Fishberg.

The author has observed one patient through an uneventful pregnancy two and one-half years after a classical acute glomerulonephritis. During the acute stage of the nephritis the blood pressure was 170/110 and convulsions occurred. Another patient who had had a classical acute nephritis in 1920 was aborted and sterilized in 1928. She was pregnant in 1923, 1925, and 1928 and uremia developed with each pregnancy. Death occurred in 1930. The autopsy confirmed the diagnosis. Many other patients with histories of previous acute nephritis have been studied. Renal impairment may or may not be present.

It is obvious that if acute nephritis may be of only a few days' or weeks' duration, many of our cases of preeclampsia and eclampsia should be so classified. Furthermore, if there are varying degrees of nephrosis, as determined by the degree of edema and albuminuria and the level of the serum protein concentration, it is obvious that many of our pre-eclamptic patients have a nephrosis. If pregnancy can be considered the etiologic agent of nephritis, then the high incidence of permanent vascular renal damage noted by various observers, especially in pre-eclamptic patients who are treated expectantly for weeks, may be attributed to the nephritis. Repeated examinations of the urine, especially microscopic examination of the sediment, are necessary to diagnose properly the condition. In certain cases, serum protein determinations will be of inestimable value.

DIAGNOSIS

The differential diagnosis of acute glomerulonephritis or lipoid nephrosis from preeclampsia is difficult. Acute nephritis and nephrosis occur more commonly in the first half of pregnancy, in contrast with preeclampsia, which occurs in the last trimester. The edema in preeclampsia may be general, but, as a rule, it differs in that it tends to be in the dependent portion of the body. In the toxemias of pregnancy the edema may disappear with proper treatment, while in the acute nephritis and nephrosis it is, on the whole, more resistant to treatment. After delivery there is a rapid elimination of the edema in preeclampsia and eclampsia which does not occur in the other conditions. The persistence of erythrocytes in the urine for longer than one week would exclude a preeclampsia. The excretion of protein in the urine in preeclampsia and eclampsia rarely exceeds 10 gm. per day, and is usually less than 5 gm. per day. In the presence of an oliguria the concentration may reach 5 per cent. In acute nephritis and nephrosis the protein excretion is quite marked, uninfluenced by treatment and especially not decreased by delivery. A serum protein concentration of less than 5 per cent before delivery, or of less than 5.5 per cent two weeks after delivery, would strongly suggest a nephrosis.

TREATMENT

Edema.—Diuretics have been of little value during pregnancy. A diet consisting of fruits and fruit juices has given excellent results, but should not be used longer than ten days. If there is a hydrothorax and ascites, the intake, especially if the fruit juice diet is used, should be limited to 1,000 or even 800 c.c. per twenty-four hours. The maintenance diet should contain as little sodium and chloride as possible. Sodium sulphate by mouth as a hydragogue cathartic is nontoxic and just as efficacious as magnesium sulphate. If the patient's serum protein is less than 5 per cent, or the serum albumin is less than 2.5 per cent,

transfusions of blood or plasma are indicated. Intravenous injections of gum acacia may be necessary to raise the oncotic pressure above the edema level. Thyroid extract has been of no value.

Proteinuria.—The protein found in the urine is chiefly albumin. No therapy has prevented or reduced its elimination. Sufficient protein should be ingested to supply the basal need, as well as to balance that lost in the urine. Carbohydrate spares protein; therefore, the caloric need should be supplied chiefly by it. It is usually difficult to force these patients to consume enough of the diet to be of any value. Vitamins B and G have been of some value in stimulating the appetite and aiding absorption.

Hematuria.—If the hemoglobin decreases below 11 gm. per 100 c.c. of blood, transfusions and iron salts are indicated.

Hypertension, Oliguria, Convulsions.—The usual treatment for eclampsia, namely, hypertonic glucose or sucrose, phenobarbital sodium, magnesium sulphate solution intramuscularly, morphine, chloral hydrate and, occasionally, venesection and lumbar puncture, should be instituted.

Pregnancy.—Pregnancy should be terminated if the symptoms and signs increase in severity. It should be interrupted without hesitation, as soon as it can be done safely, if there is no improvement in the nephritis or nephrosis, unless the addition of two or three weeks of intrauterine life will offer the baby a better chance of survival. It must be remembered that if the pregnancy is permitted to continue, intrauterine death and abortion are likely to occur. If a patient has had an acute nephritis and has recovered completely, as indicated by a negative urinalysis and normal renal function test, there is no reason why she should not be permitted to become pregnant, or if pregnancy occurs, why it should not be permitted to continue.

CONCLUSIONS

1. Acute glomerulonephritis and lipoid nephrosis of the classical type are rare complications of pregnancy. The incidence is less than 0.05 per cent.
2. These conditions are found most frequently in young primiparas in the first half of pregnancy.
3. Spontaneous abortion is a frequent occurrence.
4. Therapeutic abortion is indicated if the disease is present before the thirtieth week of pregnancy and shows no improvement in a period of two weeks. If it occurs after this time, temporization is warranted in an endeavor to obtain a viable baby.
5. The chief difference between classical glomerulonephritis and pre-eclampsia is the persistence of the hematuria in the former, and the rapid amelioration of the other symptoms after delivery in the latter.

6. Lipoid nephrosis differs from preeclampsia, as a rule, only in the degree of the various symptoms. After delivery the symptoms and signs of the former persist, while in the latter they subside.

7. Careful and repeated microscopic examinations of the sediment of the urine (Addis technic) from toxemic patients is of inestimable value in making a proper diagnosis.

8. A history of acute glomerulonephritis or lipoid nephrosis is not a contraindication to pregnancy, provided complete recovery has occurred.

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THE LOW OR CERVICAL CESAREAN SECTION*

AN ANALYSIS OF THE END-RESULTS OF AN ADDITIONAL 166 OPERATIONS

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ABDOMINAL delivery through the lower uterine segment was proposed by Frank, of Cologne, in 1907, because of his dissatisfaction with the results of the classical cesarean section, especially in women who had been long in labor and were infected or presumably infected. While this method soon found adherents in Germany, it received but little consideration elsewhere. In the United States, this procedure was seldom mentioned until 1915. Since then it has become firmly established as a standard procedure and has replaced or is gradually replacing the classical or corporeal cesarean section in many important obstetric clinics. My own interest was aroused early. At first I reserved the cervical operation for the poor risks and for the neglected cases, performing the classical operation on those women who were considered to be in good condition for an abdominal delivery. As time went on it became possible to observe repeatedly that the neglected parturient, delivered through the lower segment, convalesced much more satisfactorily than did her fellow patient considered a good surgical risk and delivered by the Sanger operation. It was equally noticed that following the low or cervical cesarean section high thermic elevation, high pulse rate, and

*Read before the Los Angeles Obstetrical and Gynecological Society, December 11, 1935.

abdominal distention—conditions which were frequently met after the classical cesarean section—were the exception rather than the rule. With these points clearly in mind, it was decided to give all women who needed an abdominal delivery the benefit of this newer method, and it has been employed consistently since.

My previous publications have emphasized that the lower uterine segment may be reached in one of three ways in performing cesarean section: (1) by the extraperitoneal route as in the Latzko operation; (2) by the transperitoneal route, sometimes referred to as peritoneal exclusion, illustrated by the Veit-Fromme-Hirst technic; and (3) by the intraperitoneal approach as in the popular method of doing the low or cervical cesarean section today. This last operation, as it is now executed, has reached its present stage of perfection through several additions and modifications in technic by numerous obstetricians. Unfortunately space does not permit me to mention all their names. Suffice it to say that in its performance the bladder is separated from the uterus, an upper flap of peritoneum may or may not also be separated, an incision is made in the lower uterine segment, and after delivery the sutured lower segment incision is entirely covered by the bladder so that it becomes retrovesical, retroperitoneal, or subperitoneal, whichever term one prefers to use.

In September, 1926, I¹ presented a paper entitled "The Obstetric Future of Women Delivered by the Low or Cervical Cesarean Section," at the Chicago meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons. Up to that time a longitudinal incision in the lower portion of the uterus had always been used. Forty-one repeated cervical cesarean sections with firmly healed scars and the impossibility of locating the previous line of incision were reported. The first patient admitted to my service for a repeat cervical cesarean section, upon my return, had been in hard labor for eleven hours. A longitudinal incision of the segment had been made at her previous intervention and, because of a large fetus, the incision had been extended upward in the body of the uterus. Upon reopening the abdomen by resecting the previous abdominal scar and upon again separating the bladder, a weak spot, about 3 cm. in circumference, was found in that part of the incision which had extended in the musculature, the edges of the scar in that area being separated and held only by peritoneum, while the lower part of the incision which had been placed in the lower uterine segment was intact and perfectly healed. A longitudinal incision was then made, and during its closure the defective portion of the scar was repaired; finally the bladder peritoneum was sutured to the uterus in such a way as to cover completely the incision.

On the basis of these findings it occurred to me that if under any and all circumstances an incision could be placed entirely in the lower segment, the incidence of weak scars could be even more definitely reduced.

Kehrer, in 1881, was said to have advised a transverse incision. Kerr and Hendry² reported 107 conservative cesarean sections by the lower segment incision. They state: "The uterine incision described in this article is made in a transverse direction so that there is ample space in which to open the lower uterine segment without disturbing the bladder." To avoid damage to the large vessels at the side of the uterus they advise curving the incision with the convexity directed downward. Anatomically, and according to their illustrations, the incision is placed above the bladder attachment on the uterus, therefore at the isthmus or junction of the lower segment and corpus rather than in the lower segment itself. My own experience has taught me that the zone of the lower segment cannot be reached definitely without separating the bladder.

The operation which I have described as the transverse cervical cesarean section^{3, 4} was devised in 1926. In this operation the bladder is separated from the uterus, a curved (half moon) incision with the convexity directed toward the symphysis pubis is placed entirely in the lower segment and is covered subsequently completely by the bladder. The transverse cervical cesarean section offers certain definite advantages, namely: (1), it avoids encroaching upon the uterine musculature and allows the placing of the incision entirely in the lower segment; (2), the bladder separation does not have to be carried as far downward as is the case with the longitudinal incision; and (3), repeated operations are simpler to perform.

M. Reeb,⁵ of Strasburg, a protagonist of the low cesarean section, recently stated in a paper entitled "À propos des fistules urinaires après la césarienne basse" that in the 415 low cesarean sections performed at the Strasburg clinic since 1908 he had observed three urinary fistulas, two vesicocervical and one vesicovaginal.

CERVICAL CESAREAN SECTIONS

TABLE I. TYPE OF OPERATION

Transverse cervical cesarean section	160
Peritoneal exclusion (Veit-Fromme-Hirst)	6
	166

TABLE II. NUMBER OF PREGNANCIES

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
Para i	55	5
Para ii	48	1
Para iii	36	
Para iv	9	
Para v	4	
Para vi	5	
Para viii	1	
Para x	2	
	160	6

These followed repeated cesarean sections in two cases and the third was complicated by a paravesical cyst injured during the intervention. Secondary operation was successful in all three cases and healing took place by first intention. In his paper the author asks if modification of technic, giving up a laborious separation of the bladder, substituting eventually, in cases of repeated cesarean, a transverse incision for the usual longitudinal, would not make these lesions even more infrequent.

Thus far, in my hands, urinary fistulas, following the low or cervical cesarean section, have not occurred. I feel strongly, however, that if a

TABLE III. LABOR

TRANSVERSE CERVICAL FORTY-THREE PATIENTS HAD LABOR			PERITONEAL EXCLUSION SIX PATIENTS HAD LABOR		
HOURS	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION	HOURS	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
2 $\frac{3}{4}$	1		22	1	
3	2		23		1
4	4		24	2	
6	3		25	1	1
7	2		26	2	
8	2		27	1	
9	2		29 $\frac{1}{2}$	1	
11	1		32		1
12	1	2	36	1	
14	1		38 $\frac{1}{2}$	1	
15	1		39	1	
17	1		48	1	
18	1	1	Few hours	1	
19	1		Slight labor	1	
20 $\frac{1}{2}$	1		Vague labor	4	
21	1				

TABLE IV. MEMBRANES

HOURS RUPTURED	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION	HOURS RUPTURED	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
2	1		17	1	
2 $\frac{3}{4}$	1		18	1	
7 $\frac{1}{4}$	2		21	1	
8	1		23	1	
10	1		24	1	1
11	1		26	1	
12	1		32		1
15	1		48		1
Few hours	2		Hours not de- termined	4	

Membranes ruptured in 3 patients of the peritoneal exclusion group.

Membranes ruptured in 21 patients of the transverse cervical group.

transverse incision makes a repeated operation easier, a point which I have frequently emphasized, and if it avoids bladder injuries on account of the less laborious separation of this organ, by the same reasoning these advantages should apply to the first or initial low cesarean section.

I have personally performed 584 cervical cesarean sections using all the methods of approach to the lower uterine segment. The first 418 were reported in a paper read before the American Association of Obstetricians, Gynecologists and Abdominal Surgeons at the Niagara Falls

TABLE V. CERVICAL DILATATION

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
Fully dilated	2	
Half dilated	1	2
Dilated to admit 4 fingers	1	
Dilated to admit 3 fingers	5	
Dilated to admit 2 fingers	5	2
Dilated to admit 1 finger	7	
Dilatation not stated		2
	<u>21</u>	<u>6</u>

In the other 22 women who had labor and who were delivered by the transverse cervical cesarean section, the amount of cervical dilatation was not noted.

TABLE VI. VAGINAL EXAMINATIONS

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
2 Vaginal examinations at home		1
1 Vaginal examination at home	1	
1 Vaginal examination in hospital	3	2

Eight vaginal examinations were done on 7 patients. The small number of vaginal examinations is accounted for by the fact that I conduct my own labor cases by means of rectal examinations and that the same rule is enforced on my service.

TABLE VII. INDICATIONS

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
Previous cervical cesarean section	63	
Previous classical and cervical cesarean sections	1	
Previous classical cesarean section	5	
Cephalopelvic disproportion	35	4
Central placenta previa	7	
Marginal placenta previa	2	
Abruptio placentae	2	
Previous vaginal plasties and uterine suspension	10	
Previous vaginal plasties (Including cervical amputation)	4	
Repaired complete perineal laceration	3	
Toxemia of pregnancy	2	
Chronic nephritis	1	
Mitral heart disease	6	
Cervical dystocia	6	1
Myomectomy during pregnancy	2	
Myomectomy, multiple	1	
Frank breech, generally contracted pelvis	5	
Spondylolisthetic pelvis	1	
Nagele pelvis	1	
Congenital hip disease	1	
Dystocia-dystrophy syndrome	2	
Justo-minor pelvis		1
	<u>160</u>	<u>6</u>

NOTE: In several of these patients there was more than one indication. Only what was thought to be the most important indication was noted in this table. The indication was a previous cesarean section in 69 or 43.1 per cent of the patients.

meeting in September, 1930.⁶ The cervical scars of four uteri, later removed for other pathologic conditions, likewise were studied and reported.⁷

Since reporting the first 418 cervical cesarean sections which had been performed in 31 hospitals, 166 additional operations, 160 trans-

TABLE VIII. ANESTHESIA

TYPE OF ANESTHESIA	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
Local	17	
Spinal	3	
Avertin, nitrous oxide, oxygen	65	1
Avertin and local	1	
Nitrous oxide, oxygen, ether	74	5
	<u>160</u>	<u>6</u>

NOTE: For local anesthesia 1 per cent novocaine solution was used. For spinal anesthesia 120 mg. of novocaine crystals dissolved in spinal fluid were employed. The dose of avertin varied from 60 to 100 mg. per kilo of body weight. The average dose was 80 mg. This form of anesthesia is contraindicated in hepatic and renal disorders.

TABLE IX. COMPLICATIONS

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
<i>Preoperative:</i>		
Upper respiratory tract infection	1	
Anemia of pregnancy (severe)	1	
Ablation of ovarian cyst with twisted pedicle during pregnancy	1	
Myomectomy for necrobiosis during pregnancy	1	
	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
<i>Postoperative:</i>		
Sepsis of abdominal incision	5	1
Lochiometra	4	2
Pyelitis	4	1
Pyelitis and vesical distention	1	
Gastric dilatation requiring lavage	3	1
Upper respiratory tract infection	5	
Phlebitis (left)	5	
Puerperal psychosis	1	
Alveolar abscess, Temp. 105° F.	1	
Puerperal sepsis, Temp. 105° F.	1	
Frontal sinusitis and carious tooth	1	
Dehiscence of abdominal incision	1	
Blood transfusion was resorted to six times on five patients.		

verse cervical cesarean sections and 6 Veit-Fromme-Hirst peritoneal exclusions have been performed in 21 hospitals. Peritoneal exclusion is resorted to in women who have had long labors, ruptured membranes, vaginal examinations, and sometimes attempts at delivery by forceps. The 166 operations mentioned form the basis of this paper, and, for the sake of clearness, are presented in tables.

CASE REPORT

One patient in this group has an interesting history. Mrs. M. F., forty years old, para xii. Her first child, a male infant, was delivered normally in her home in 1917 and died at four and one-half months. A female child was delivered normally in her home a year later. Her third child, a ten-pound boy, and her fourth child, a female infant, were also delivered normally in her home. The fifth pregnancy ended in an eight weeks' miscarriage which was followed by a curettage. She was admitted to my service at the end of her sixth pregnancy. She was then twenty-nine years of age. She had a hemorrhage from a partially separated placenta and was not in labor. On Aug. 30, 1922, she was delivered by a Veit-Fromme-Hirst peritoneal exclusion of a female child who lived. Her puerperium was complicated by gastric dilatation and a myocardial disorder; she nonetheless made a good

TABLE X. MATERNAL MORTALITY

There was one maternal death in 166 cases or 0.6 per cent. This patient was a quartigravida, her first pregnancy having terminated in a miscarriage and her second in the delivery of a macerated fetus. Her third pregnancy was complicated by chronic nephritis, edema, and asthma. She was delivered on April 17, 1931, by a transverse cervical cesarean section of a male child who did well. During her fourth pregnancy she developed a hernia of the gravid uterus, the chronic nephritis and emphysema became accentuated, a second transverse cervical cesarean section was performed at term, on Aug. 11, 1932, and she was again delivered of a male child who lived. On August 12 she developed a paralytic ileus which was controlled by a jejunostomy performed under local anesthesia. She died of chronic nephritis, bronchitis, emphysema, and myocarditis thirty-six hours after operation.

TABLE XI. BABIES

169 babies were born, there being 3 sets of twins. Of these 78 were males and 91 females.

One male child had spina bifida and was operated on successfully. One male child weighed 13 pounds 13 ounces (6,298.5 grams).

Fetal Mortality

169 babies were born, 8 of whom did not survive, an uncorrected fetal mortality of 4.7 per cent. This includes monsters, macerated fetuses, and stillborns.

Causes of Fetal Deaths

1. Macerated male fetus, second cervical cesarean.
2. Stillborn, male, autopsy showed congenital heart disease. First cervical cesarean. (Mother was 46 years old and had had extensive vaginal plastics and uterine suspension.)
3. Stillborn, female, central placenta previa. First cervical cesarean.
4. Underdeveloped male (2,250 grams); lived 24 hours. Second cervical cesarean.
5. Female twin, died of hemorrhagic disease. Third cervical cesarean.
6. Premature male, 8 months' gestation, lived 6 hours. Second cervical cesarean.
7. Premature female, 7 months' gestation, lived 4 hours. Fourth cervical cesarean.
8. Female monster (absence of anterior abdominal wall). Second cervical cesarean.

All the fetal deaths occurred in the transverse cervical cesarean group.

TABLE XII. REPEATED CERVICAL CESAREAN SECTIONS

Second operation	44
Third operation	20
Fourth operation	4
Sixth operation	1
	<hr/> 69

NOTE: In 5 of these cases the previous operation was a classical cesarean section performed by other surgeons. In the other 64 cases the previous operation was a cervical cesarean section.

A transverse cervical cesarean section may be done in subsequent deliveries, but the Veit-Fromme-Hirst peritoneal exclusion cannot be repeated.

recovery. Following this cesarean section she had three normal deliveries in the hospital, female children being born. She was admitted at the end of her tenth pregnancy with a placenta previa and hemorrhage and she was not in labor. She was delivered of a male child the same day, April 3, 1931, by a transverse cervical cesarean section, under local anesthesia. The lower segment was found intact and

TABLE XIII. PREVIOUS SCARS

SIXTY-NINE SCARS EXAMINED	
<i>Cervical Cesarean Scars</i>	
Cervical scar could not be identified in	54
Scar appeared as a hair line in	1
Scar appeared as a thin line in	3
Lower segment firm but irregular in areas in	1
Lower segment intact but thin in	1
Lower segment healed but thin at midpoint in	1
(This was the sixth cervical cesarean)	
<i>Classical Cesarean Scars</i>	
Previous classical cesarean scars encountered	8
Weak scar	1
Healed scars	7
All the healed scars appeared as depressions in the uterine wall.	
There were no ruptured scars in this series of cases.	

TABLE XIV. ADHESIONS IN THE REPEATED CERVICAL CESAREAN SECTIONS

Following the Veit-Fromme-Hirst peritoneal exclusion, a wide band of peritoneum extends from the cervix to the abdominal wall.

In the transverse cervical cesarean group 30 had adhesions as follows:

Lower segment adherent to abdominal wall	3
Bladder adherent to parietal peritoneum	7
One peritoneal band to abdominal wall	7
Two peritoneal bands to abdominal wall	4
Three peritoneal bands to abdominal wall	1
One omental adhesion	8

No intestinal adhesions were found in any of the patients.

TABLE XV. PELVIC DELIVERIES FOLLOWING THE CERVICAL CESAREAN SECTION

	TRANSVERSE CERVICAL	PERITONEAL EXCLUSION
One normal delivery	1	
(Seven months' macerated fetus)		
Two normal deliveries	2	
Three normal deliveries		1
Version and extraction	1	
(Twelve-hour labor)		
Miscarriage at 5 months	1	
Eight deliveries through the pelvis; six children survived.		

TABLE XVI. SUBSEQUENT OPERATIONS

1. Supravaginal hysterectomy, right salpingo-oophorectomy for a necrotic myoma.
2. Supravaginal hysterectomy, right salpingo-oophorectomy for necrotic cystic myoma and cystic right ovary.
3. Ablation of ovarian cyst with twisted pedicle during the sixth week of the third pregnancy. Two previous transverse cervical cesarean sections. Pregnancy went to term. Delivery by third transverse cervical cesarean section.
4. Vaginal plastics, supravaginal hysterectomy, double salpingo-oophorectomy for procidentia. Appendectomy.
5. Left salpingo-oophorectomy for endometriosis.
6. Porro cesarean section, right salpingo-oophorectomy for hemorrhage from placenta previa at second pregnancy.

contained no weak areas. Subsequent to the second cesarean section she had two normal deliveries in the hospital, resulting in the birth of a male and a female child, the last delivery occurring in 1934. She now has 10 living children, 3 boys and 7 girls.

SUMMARY AND CONCLUSIONS

This study is based on 166 additional cervical cesarean sections, 160 transverse cervical cesarean sections and 6 Veit-Fromme-Hirst peritoneal exclusions. They follow a previously published report of 418 cervical cesarean sections.

These 166 operations were performed by the author in 21 hospitals, varying in equipment from that of the well-regulated metropolitan maternity hospital, where a separate operating room is frequently maintained for cesarean section, to that of the small rural hospital where all surgery, clean and septic, including cesarean section, is performed in the same operating room.

Increasing evidence seems to prove that the cervical cesarean section fulfills the three main considerations advanced for it by its protagonists, namely: protection against septic peritonitis, better healing of the incision, and an easier convalescence.

There was one maternal death in the 166 operations, a gross maternal mortality of 0.6 per cent. This occurred in a quartigravida at her second cervical cesarean section. The cause of death was chronic nephritis, bronchitis, emphysema, and myocarditis.

One hundred and sixty-nine infants were born, 78 males and 91 females; 8 did not survive, an uncorrected fetal mortality of 4.7 per cent. This includes monsters, macerated fetuses, and stillborns (Table XI).

The cervical cesarean section may be repeated with ease. The highest number performed on one woman in this series was 6 (Table XII).

In 61 repeated cervical cesarean sections no ruptured scars were encountered and no intestinal adhesions were discovered.

There were 8 pelvic deliveries in 5 women. Six of the infants survived, 1 fetus was macerated, the other was a five months' miscarriage.

The transverse incision, in my hands, has proved to be more satisfactory than the longitudinal in performing the low or cervical cesarean section.

An adequate test of labor may be safely given in border line cases, thus allowing a number of women to deliver themselves through the pelvis who otherwise might have been delivered abdominally.

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PELVICEPHALOGRAPHY

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THE information obtained from the usual methods of roentgen pelvimetry and fetal cephalometry has been a disappointment to many obstetricians and radiologists. The reasons for this are probably numerous, but mainly it has likely been due to a failure to consider the third dimension. The relationship between the fetal cranium and the birth canal is best visualized by volumetric comparison. The problems in the mechanism of labor cannot be reduced to the simplicity of comparing a fetal skull diameter to a pelvic diameter. Another factor of consequence is the manner of interpretation of roentgenographic data. It must be borne in mind that these data are only additional information which may be utilized in handling a particular case.

It has been emphasized by Thoms³⁶ and others ³³ that external pelvimetry has only a relative value in determining the internal pelvic diameters. Since the birth canal has a direct relationship to the internal pelvic diameters, it is necessary to measure it to know its volume capacity. It is seldom possible by external means to obtain any definite idea of the mass volume of the fetal skull. Therefore, a roentgenographic method which will measure the three dimensional size of the fetal skull and the birth canal should be of aid to the obstetrician.

The author has described such a method which requires only two exposures and does not require any measurements of the patient.¹⁻³ All of the data are obtained from roentgenograms in the anteroposterior view with the patient in supine position and lateral view with the patient in lateral recumbent position. If preferred, the exposures may be made with the patient standing. Also, by one additional exposure in the anteroposterior view, the films may be examined stereoscopically. The accuracy of the method has been within 5 per cent error for linear measurements and 10 per cent for volumetric estimations. All types of presentations are measurable and the examination may be done with accuracy from the thirtieth week of gestation. In breech presentations additional exposures are, of course, necessary to measure the fetal skull.

The volume of the fetal cranial skull is determined by measuring the circumference of the film images. The mean circumference measurements of a spheroid can be used to calculate its volume (Table I). The circumference measurement eliminates error due to oblique positions of skull diameters in relation to the film and makes it possible to measure all cases. The magnification of the film image is corrected by a calculator

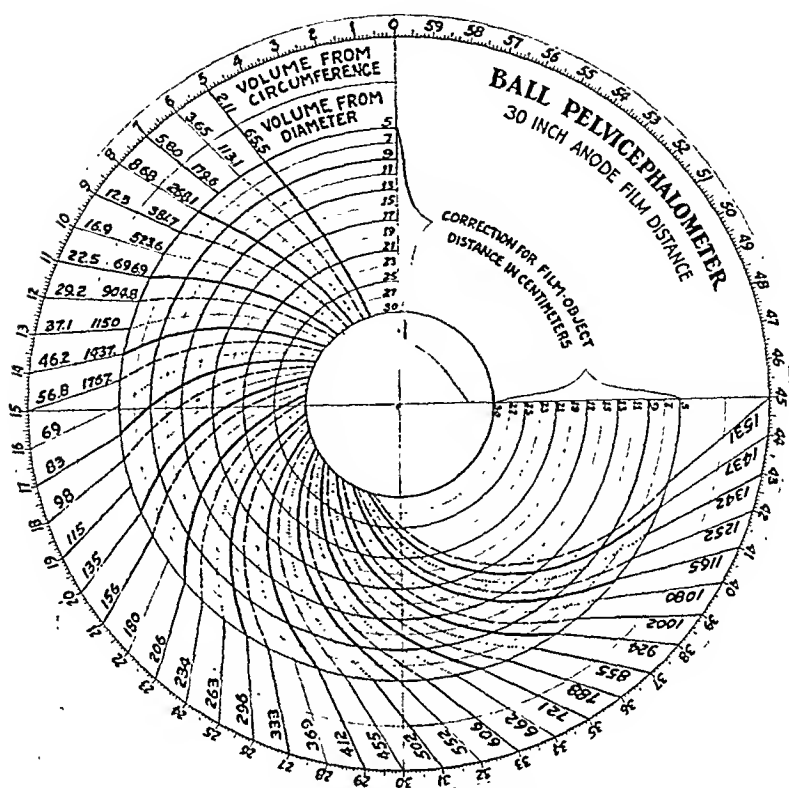


Fig. 1.—A chart for the correction of two variables, which is the dial of the pelvicephalometer.

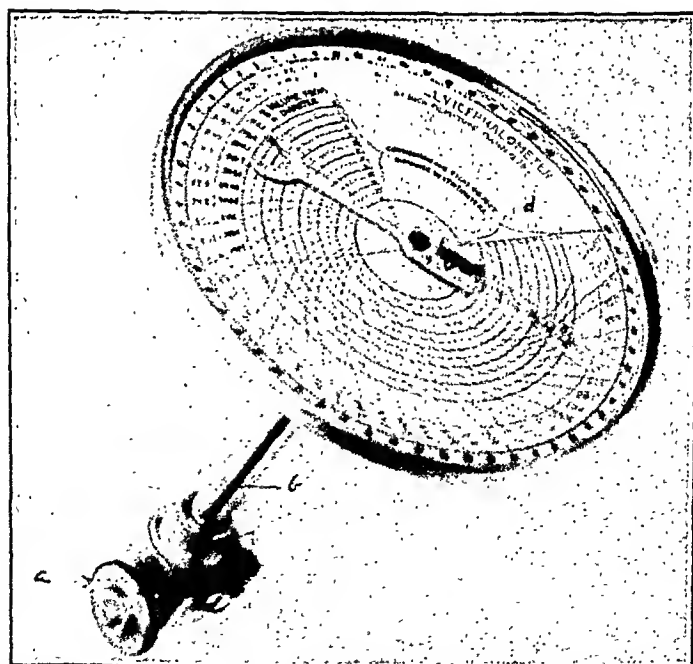


Fig. 2.—The pelvicephalometer. A calibrated wheel (a) is traced over the perimeter of the skull image. A shaft inside casing (b) is connected with pointer (c) which travels over correction chart (d).

(correction chart) (Fig. 1), thereby eliminating any mathematical computation. To conveniently obtain measurements, a correction chart was mounted on a dial and the pointer geared to a calibrated contact wheel similar to a map measure, Fig. 2. Two tables showing the volume of a sphere from a circumference measurement (Table I) and volume from a diameter measurement (Table II) are placed on the calculator

TABLE I. SHOWING THE VOLUME OF A SPHERE FROM CIRCUMFERENCE MEASUREMENT

CIRCUMFERENCE	VOLUME	CIRCUMFERENCE	VOLUME
15.0 cm.	56.8 c.c.	33.0 cm.	606.0 c.c.
15.5 cm.	62.8 c.c.	33.5 cm.	636.0 c.c.
16.0 cm.	69.0 c.c.	34.0 cm.	662.0 c.c.
16.5 cm.	75.7 c.c.	34.5 cm.	693.0 c.c.
17.0 cm.	83.0 c.c.	35.0 cm.	721.0 c.c.
17.5 cm.	90.5 c.c.	35.5 cm.	755.0 c.c.
18.0 cm.	98.0 c.c.	36.0 cm.	788.0 c.c.
18.5 cm.	106.5 c.c.	36.5 cm.	820.0 c.c.
19.0 cm.	115.4 c.c.	37.0 cm.	855.0 c.c.
19.5 cm.	125.0 c.c.	37.5 cm.	889.0 c.c.
20.0 cm.	135.0 c.c.	38.0 cm.	924.0 c.c.
20.5 cm.	145.1 c.c.	38.5 cm.	961.0 c.c.
21.0 cm.	156.4 c.c.	39.0 cm.	1,002.0 c.c.
21.5 cm.	168.0 c.c.	39.5 cm.	1,042.0 c.c.
22.0 cm.	180.0 c.c.	40.0 cm.	1,080.0 c.c.
22.5 cm.	192.2 c.c.	40.5 cm.	1,122.0 c.c.
23.0 cm.	205.8 c.c.	41.0 cm.	1,165.0 c.c.
23.5 cm.	218.0 c.c.	41.5 cm.	1,204.0 c.c.
24.0 cm.	233.5 c.c.	42.0 cm.	1,252.0 c.c.
24.5 cm.	248.5 c.c.	42.5 cm.	1,293.0 c.c.
25.0 cm.	263.0 c.c.	43.0 cm.	1,342.0 c.c.
25.5 cm.	280.0 c.c.	43.5 cm.	1,390.0 c.c.
26.0 cm.	296.0 c.c.	44.0 cm.	1,437.0 c.c.
26.5 cm.	314.0 c.c.	44.5 cm.	1,487.0 c.c.
27.0 cm.	333.0 c.c.	45.0 cm.	1,531.0 c.c.
27.5 cm.	350.0 c.c.	45.5 cm.	1,588.0 c.c.
28.0 cm.	369.0 c.c.	46.0 cm.	1,640.0 c.c.
28.5 cm.	389.0 c.c.	46.5 cm.	1,692.0 c.c.
29.0 cm.	412.0 c.c.	47.0 cm.	1,746.0 c.c.
29.5 cm.	433.0 c.c.	47.5 cm.	1,803.0 c.c.
30.0 cm.	455.0 c.c.	48.0 cm.	1,867.0 c.c.
30.5 cm.	478.0 c.c.	48.5 cm.	1,922.0 c.c.
31.0 cm.	502.0 c.c.	49.0 cm.	1,982.0 c.c.
31.5 cm.	524.0 c.c.	49.5 cm.	2,044.0 c.c.
32.0 cm.	552.0 c.c.	50.0 cm.	2,105.0 c.c.
32.5 cm.	578.0 c.c.		

TABLE II. SHOWING THE VOLUME OF A SPHERE FROM A DIAMETER MEASUREMENT

DIAMETER	VOLUME	DIAMETER	VOLUME
5.0 cm.	65.45 c.c.	10.5 cm.	606.13 c.c.
5.5 cm.	87.11 c.c.	11.0 cm.	696.91 c.c.
6.0 cm.	113.10 c.c.	11.5 cm.	796.33 c.c.
6.5 cm.	143.79 c.c.	12.0 cm.	904.78 c.c.
7.0 cm.	179.59 c.c.	12.5 cm.	1,022.70 c.c.
7.5 cm.	220.89 c.c.	13.0 cm.	1,150.3 c.c.
8.0 cm.	268.08 c.c.	13.5 cm.	1,288.2 c.c.
8.5 cm.	321.56 c.c.	14.0 cm.	1,436.8 c.c.
9.0 cm.	381.70 c.c.	14.5 cm.	1,596.3 c.c.
9.5 cm.	448.92 c.c.	15.0 cm.	1,767.1 c.c.
10.0 cm.	523.60 c.c.		

for quick reference and compactness. To the corrected measurement of the perimeter of the fetal cranial skull, 2 cm. are added to allow for the volume of the scalp.

The fetal skull volume is compared to the volume capacity of two pelvic diameters, the true conjugate and the bischial spine. These diameters are chosen because one of the two will always be the smallest pelvic diameter, except in the true funnel pelvis, and the planes of these diameters are parallel to the film when the exposures are made, thereby eliminating obliquity and error in measurement. The pelvic diameter, as measured on the film, is corrected for its magnification by use of the calculator. The linear measurement of the diameter is then interpolated into volume capacity by reference to Table II. Thus the fetal skull volume can be compared to the volume capacity of both or the smallest pelvic diameter. The ratio of the mass volume of the "passenger" to the volume capacity of the "passage" is then expressed in units of volume, milliliters.

The interpretation of a measured disproportion and how it might interfere with a normal spontaneous delivery is naturally subject to data from a large series of cases. Some observations which have been made will be mentioned. Before doing so, however, it is better to discuss briefly the architecture of the pelvis.

The birth canal of the female pelvis is usually described as being cylindrical or ovoid when the walls are compressed anteroposteriorly or laterally. Pelves have many classifications, the majority of which show a great knowledge of descriptive adjectives. A truly descriptive and workable classification of pelvises is that of Caldwell and his associates,^{9, 10} which is an excellent presentation of the anatomical variations in the bony female pelvis. Moloy and Swenson have attempted by roentgenographic studies to correlate the type pelvises with the mechanism of labor. By whatever classification, including pathologic pelvises, it should be remembered that the smallest pelvic diameter is the true conjugate or bischial spine, except in the true funnel pelvis, and that, for delivery, the fetal head must pass through the smallest pelvic diameter. In the platypelloid (flattened) pelvis the bischial spine diameter will measure more than the true conjugate; and, conversely, in the android pelvis the true conjugate is greater than the bischial spine diameter. An important question is whether the transverse diameter of the plane of the pelvic inlet is ever smaller than the bischial spine diameter (bony tumors excepted), or if the anteroposterior diameter of the plane at the level of the bischial spines is ever smaller than the true conjugate diameter. To the first part of the question, the author has not, within the limits of his investigation, found an example of such a case. To the second part, there are possibly examples other than the true funnel pelvis, but such a case would show a marked narrowing of the sacrosciatic notch and a loss of the normal convexity of the sacrum. The

lateral roentgenogram, Fig. 3, shows the relationship of this part of the pelvis. Thus, by volumetric comparison, it is important to consider the convexity of the sacrum and the width of the sacrosciatic notch in marginal size cases.

INTERPRETATION OF VOLUME RATIO

Let us assume that a fetal cranial skull has a mean circumference measurement of 31 cm., representing a volume of 502 ml. or c.c. (Table I). We add 2 cm. to the perimeter to allow for the volume of the scalp and find that the cranial skull plus the scalp measures 606 ml. The true conjugate diameter measures 11 cm. and the biischial spine diameter 9 cm. By referring to Table II, it is seen that a sphere of a diameter

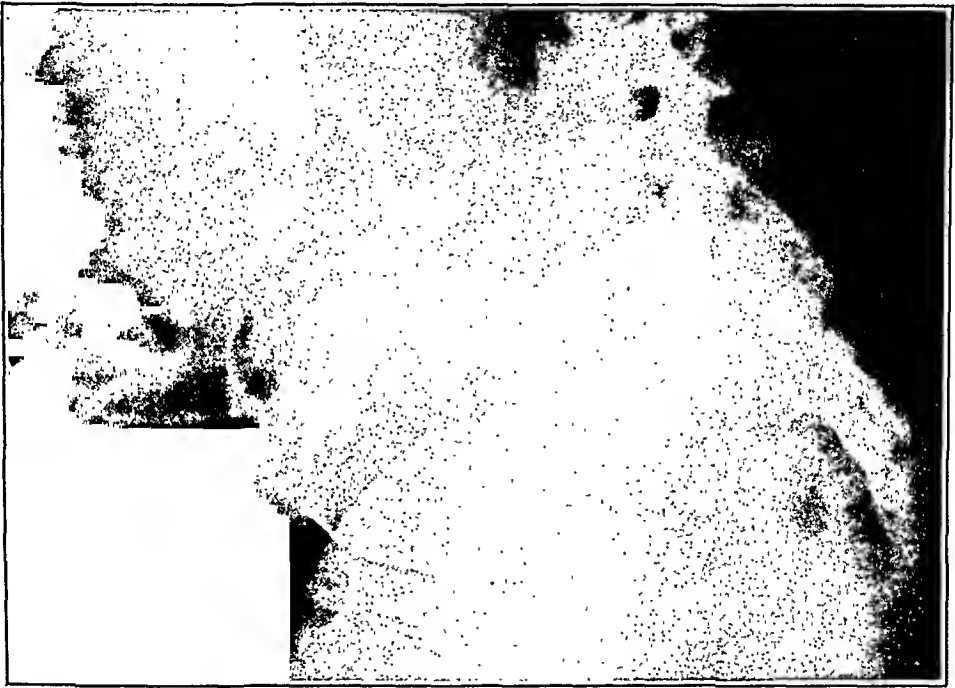


Fig. 3.—Lateral roentgenogram of the female showing a wide sacrosciatic notch and normal convexity of the sacrum.

equal to the true conjugate has a volume of 696 ml. With cephalic presentation in anteroposterior or oblique positions, the space is more than adequate. A sphere equal to the biischial spine diameter has a volume of only 381 ml., while the fetal eranium measures 606 ml., which gives an apparent disproportion of 225 ml. What will be the mechanism by which the eranium passes this pelvic diameter? If the long diameter of the head should attempt to pass in the transverse position, it will not likely get through without a fetal death because approximately 150 ml. has been found by the author to be the maximum limit of head molding without a mortality (cerebral hemorrhage). However with rotation of the head and presentation of the biparietal plane, it is the equivalent of reducing the volume of the eranium by 50 to 100 ml., since the usual difference in occipitofrontal and suboccipitobregmatic circumferences is

from 1 to 2 cm. Assuming in this case only 1 cm. difference in circumference measurements, there is yet 175 ml. more volume of the cranium than volume capacity of the diameter. The scalp volume, surprisingly enough, is 100 ml., and with a 50 per cent compressibility of the scalp, another 50 ml. is reduced from the 175, making 125 ml. that must be taken care of through molding of the head, which is a none too safe margin. However, the pelvic architecture enters into the problem, and with a full curved sacrum and wide sacrospinous arch, there is available bony space which not only permits easy rotation and adaptation of the optimal cranial diameter but also might allow the major portion of the cranium to pass posterior to the bischial spine diameter. But with a narrow notch, straight type of sacrum and small posterior pelvic capacity, the bischial spine diameter should be large enough to permit the cranium to pass it within safe limits of molding to prevent a fetal mortality. From the series of cases examined it has been found that an unengaged fetal head which measures 150 ml. greater than the volume capacity of the true conjugate diameter is a true disproportion and, with few exceptions, will result in a fetal mortality if submitted to labor. If the bischial spine diameter should be unusually large, suggesting a very wide transverse diameter of the inlet, there is the mechanical possibility of a transverse engagement of the head which would materially lessen the molding necessary to pass the superior strait, a fairly easy spontaneous delivery would be the result. It is, of course, not necessary to emphasize that the above considerations are based upon volumetric comparison and the other factors such as uterine force, etc., are to be considered.

PELVIC CLASSIFICATION WITH TYPES OF PRESENTATION

A classification of pelvis based upon the measurement of the true conjugate and bischial spine diameters has been used by the author for convenience. The true conjugate is made the numerator and the bischial spine the denominator of a fraction. When the measurements are within 5 mm., it is called a *one* pelvis because of the close proximity to unity. If the numerator is greater than 0.5 cm., it is called a *one-plus* pelvis and conversely a *one-minus* pelvis; i.e., a gynecoid pelvis with the two diameters near the same size is a *one* pelvis, a platypelloid or flat pelvis is a *one-minus*, and an android with large true conjugate and narrow bischial spine diameters is a type *one-plus*. It will be noted that there is a deficiency in this roentgenographic classification, because the width of the sacrospinous notch and curve of the sacrum has not been described. For this reason, I again emphasize the excellent classification of Caldwell and associates.

It is interesting to tabulate the type pelvis racially and as regards presentation. Table III shows the position and presentation of the

native white, and Table IV, the same in the southern negro. This is a tabulation of only 173 cases, and in a larger series, there is a possibility of some change in the figures, but it is probably representative. Table V indicates that there is no marked racial difference in fetal presentation, although Tables III and IV show considerable variation in type pelvis.

VOLUME INCREASE OF FETAL CRANIUM

The absolute rate of increase in volume of the fetal cranium in utero is represented in Fig. 4. The curve is a composite of a series of cases

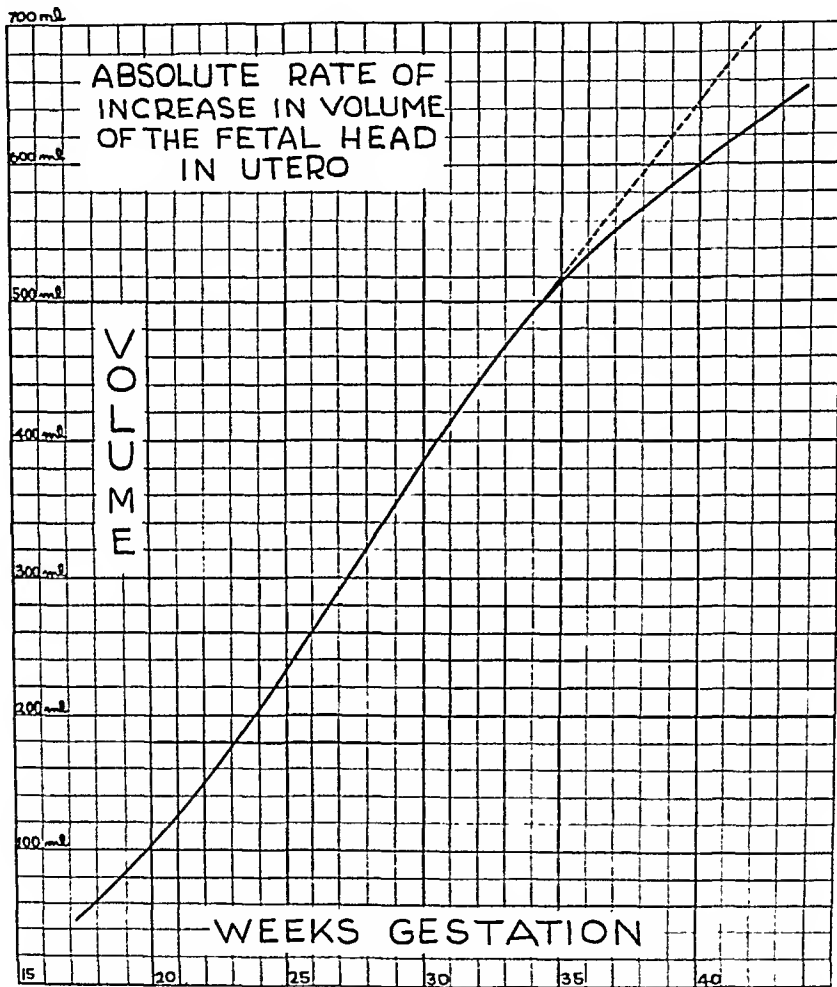


Fig. 4.—The absolute rate of increase in volume of the fetal cranium in utero as obtained from roentgenographic data. The dotted line represents the unengaged head.

examined radiographically at intervals of two to four weeks during gestation. It can be used to estimate the size of the fetal cranium at any period subsequent to the roentgenographic examination, and if it is found to be a marginal size case the examination can be advantageously repeated during labor. The author hopes this curve will be checked closely for its accuracy. It might be utilized to determine fetal death when there have been previous roentgenograms.

TABLE III. THE INCIDENCE OF TYPE Pelves WITH POSITION AND PRESENTATION OF THE FETUS IN THE NATIVE SOUTHERN WHITE

POSITION AND PRESENTATION	TYPE Pelves WHITE			TOTAL
	1	1-	1+	
Breech	3.0	0.0	4.0	7.0
Transverse	0.0	1.0	0.0	1.0
L. O. A.	11.0	9.0	18.0	38.0
L. O. P.	2.0	2.5	3.0	7.5
L. O. T.	6.5	1.5	4.0	12.0
R. O. A.	3.0	1.0	4.5	8.5
R. O. P.	3.0	2.0	9.0	14.0
R. O. T.	5.5	1.0	5.5	12.0
Total	34.0	18.0	48.0	100.0

TABLE IV. THE INCIDENCE OF TYPE Pelves WITH POSITION AND PRESENTATION OF THE FETUS IN THE SOUTHERN NEGRO

POSITION AND PRESENTATION	TYPE Pelves COLORED			TOTAL
	1	1-	1+	
Breech	2.0	0.0	4.5	6.5
Transverse	0.0	0.0	0.0	0.0
L. O. A.	14.0	14.0	6.5	34.5
L. O. P.	8.5	0.0	0.0	8.5
L. O. T.	2.5	0.0	2.5	5.0
R. O. A.	4.5	4.5	4.5	13.5
R. O. P.	12.0	2.0	0.0	14.0
R. O. T.	6.5	4.5	4.5	15.5
L. M. T.	0.0	0.0	2.5	2.5
Total	50.0	25.0	25.0	100.0

TABLE V. A RACIAL COMPARISON OF THE FREQUENCY OF OCCIPITOPOSTERIOR, ANTERIOR AND TRANSVERSE IN PRIMIPARA AND MULTIPARA

POSITION AND PRESENTATION	WHITE		TOTAL	COLORED		TOTAL
	PRIMIP-ARAS	MULTIP-ARAS		PRIMIP-ARAS	MULTIP-ARAS	
Occipitoposterior	15.0	8.0	23.0	14.5	10.5	25.0
Occipitoanterior	26.0	25.0	51.0	29.0	21.0	50.0
Occipitotransverse	9.5	11.0	20.5	10.5	6.5	17.0
Breech	1.5	4.0	5.5	4.0	2.0	6.0
L. M. T.	0.0	0.0	0.0	0.0	2.0	2.0
Total	52.0	48.0	100.0	58.0	42.0	100.0

SUMMARY

Attention is called to a roentgenographic method of pelvimetry and fetal cephalometry which measures the volume ratio between the fetal cranium and pelvic diameters.

It is desired to emphasize that the roentgenographic data are accessory aid to the obstetrician who will think in terms of the third dimension, and that the mechanism of labor involves a volumetric consideration rather than linear measurements.

The importance of the architecture of the pelvis in the mechanism of labor in marginal sizes only is discussed briefly.

The frequency of occurrence of different type pelves with presentation and position of the fetus near term or in labor in the native southern white and colored is tabulated.

The absolute rate of increase in volume of the fetal cranium in utero as obtained from roentgenographic data is presented.

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Celentano, Pasquale: Is There a Primary Krukenberg Tumor? Arch. di ostet. e. ginec. 42: 731, 1935.

A woman twenty-four years of age complained of enlargement of the lower abdomen, having no gastric symptoms. Both ovaries and the uterus were removed. The right ovary was the size of the head of a full-term fetus; the left the size of a hen's egg. Microscopic examination showed this to be a Krukenberg tumor.

Convalescence was normal, and no gastric symptoms appeared for about seven months after operation. Four months later she died of a gastric carcinoma. Since there were no gastric symptoms until seven months after operation, might this not be a metastasis from the ovary to the gastrointestinal tract?

JAMES W. PIERCE.

Maggi, Nicolo: Bilateral Sarcoma of the Ovaries, Folia gynaeec-demograph. 32: 4, 1935.

The author describes a case of giant round cell tumor involving both ovaries in a woman thirty-two years old. A discussion of the differential diagnosis between the other common tumors of the ovaries follows. He also refers briefly to tumors of connective tissue origin.

MARIO CASTALLO

HEREDITY AS THE CAUSE OF CONGENITAL MALFORMATIONS

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FROM early times, mankind has sought in the environment the explanation for congenital malformations. The explanations have covered a wide range of possibilities.

An explanation has been advanced recently by Petersen,^{4, 5} who claims that changes in the barometric pressure at the time of conception are responsible for malformations.

Petersen states that there is a geographic variation in the appearance of malformations, those areas which are the centers of storm disturbances, or in storm tracks, having the highest number of malformations. In a later paper, he claims that there is also a seasonal variation in the appearance of malformations, more malformed children being conceived in March and April than should be on the basis of expectation, and fewer in July, August, and September than would be expected. He found April and March to have the greatest variation in barometric pressure in the region from which he obtained his data, namely, Chicago.

Murphy,⁶ investigating the records for Philadelphia, found that the number of normal conceptions was higher in the late winter and early spring months than at other times, and that the proportion of malformations which were conceived during June, July, and August was disproportionately high; thus they were very low at the time that Petersen found them highest and vice versa. He concluded that there was no evidence, as far as Philadelphia was concerned, that alterations in barometric pressure had any causal relationship to the production of malformations. The barometric pressure in Philadelphia had varied more in January in the five years for which he investigated the conception times than it had in the other months. Dittrich⁷ found unduly high proportions of conceptions of malformed individuals in March and August, which he attributed to changes in the ultraviolet light.

It seemed rather unreasonable to conceive of malformations being caused by variations in barometric pressure, inasmuch as the ova, at least, develop in a follicle surrounded by fluid and so are immune from barometric changes. Moreover the barometric changes occurring normally are relatively slight, and as Murphy points out, rather gradual, so that it does not appear reasonable to expect that such an influence as barometric pressure would alter the course of development. Moreover, since not all children conceived in these months exhibit malformations, there must be some individual differences in the susceptibility to variations in pressure, even if that be the correct explanation. The tendency for malformations to occur in more than one child in the family, in a fair proportion of cases, would lead one to think that some inherent quality in that family was mainly responsible for the defects.

MATERIAL USED

Some years ago, I collected a large series of malformations from medical literature, most of them of the bizarre type which were obvious on inspection alone. A few which were internal defects were from cases in which the diagnosis of the malformation had been verified at operation or autopsy. This series was collected to determine the correctness of Still's⁸ statement that malformations occurred with undue frequency in first pregnancies, and were due to Nature's inexperience in producing children in that particular union. As Nature became more adept, he said, malformations grew less. This idea was shown to be erroneous (Macklin^{2, 3}), the first born being affected in proportion only to their number in the population. In one paper² is the bibliography of most of the cases which are used in this study. These references will not be duplicated here because of their length.

Conception Times.—In 256 instances, the date of the last period was mentioned, or the date of birth and the duration of the pregnancy were given. Those cases in which date of birth was given without data as to the date of the last period or the duration of the pregnancy were discarded. The months of conception for these 256 malformed individuals are shown in Table I, and although it is true that in April there were 27 conceptions, there were also 27 in February and July. The five months from September to January inclusive have the lowest number of conceptions, ranging from 14 to 18. It was impossible to attempt any correlation between barometric pressures and conception times in this series, for they were taken from records which covered a long period of years, and a wide range of geographic location. I doubt whether the high incidence of conception in February, April, and July, or the low incidence in the autumn and early winter months has any significance.

TABLE I

MONTH OF CONCEPTION	NO. OF CONCEPTIONS	PERCENTAGE
January	18	7.03
February	27	10.54
March	21	8.22
April	27	10.54
May	24	9.38
June	22	8.61
July	27	10.54
August	25	9.72
September	16	6.24
October	18	7.03
November	14	5.51
December	17	6.64
Total	256	100.00

Heredity as the Cause of Malformations.—In going over the data, two points were brought out which supported both the idea that external causes played a very subsidiary rôle, if any, in the production of

malformations, and that heredity was the important and determining factor. These two points were: (1) the occurrence of malformations in monovular and binovular twins, and (2) the fairly frequent occurrence of the same malformation, or of similar malformations in two or more children in the family. These two points will be discussed in detail, in order to give evidence in support of the idea that heredity is the causal factor.

Incidence of Malformations in Twins.—There are two types of twins: (1) those arising from two eggs, in which the sex may or may not be the same, and in which the heredity of any single trait may or may not be the same, but in which the total heredity is always different. They resemble each other no more nor less than siblings in a family, which are born at different times. (2) There are monovular twins, which are always of the same sex, and in whom the total heredity is as nearly identical as two individuals can be identical. If some cause, operating before birth, such as alteration in barometric pressure, or being the first in the family, or inadequate diet, etc., be responsible for malformations; then whenever twins are born with one showing a defect, *both twins*, whether they be monovular or binovular, should be affected. If the cause of the defect be a matter of heredity in the germ cells, then monovular twins should be alike, either both normal or both defective; but binovular twins might be different or they might be similar.

Among *binovular twins* we should expect to find one pair of like-sexed twins for every pair of mixed twins, since they occur, on the basis of chance, in the ratio of one pair of male twins to one pair of female twins to two pairs of twins of both sexes. Twins are really born in the ratio of one pair of male twins to one pair of female twins to one pair of twins of both sexes. The excess of like-sexed twins is due to the fact that identical or monovular twins are always of the same sex, and increase the number of like-sexed twins. Now, as just stated, if environmental causes be responsible for defects, then we should always find both twins defective, or both twins normal; there should never be any instances of twins where one is normal and the other affected. If, on the other hand, heredity is the cause, then we should find monovular twins always alike, with both normal or both affected; but in the case of binovular twins they might be both normal, both affected, or one normal and one affected. Investigation of malformations in twins should therefore prove fruitful for ascertaining the relative rôles of environment and heredity as the cause of the defects.

One more point should be brought out. If we do find instances in which one of a pair of twins is normal, while the other is affected, such cases should be all binovular, and if the series is large enough, we should expect to find one pair of male twins to one pair of female twins to two pairs of mixed twins. On the other hand, in those instances

in which *both* twins are affected, we should find not only those cases of binovular twins of like and mixed sex in which both were affected, but we should find *all* the cases of monovular twins, for if one is affected, both are; and moreover since they are always of the same sex, we should find a great preponderance of like-sexed twins in the group. The addition of the two groups, those with but one affected and those with both affected, should give the ratio of 1:1:1 which is found in twins in general.

Let us look at the twins which were found in the records investigated. There were 1,420 cases of malformations in the data used. In these there were 55 pairs of twins where one only was affected, and 33 pairs of twins where both were affected. The very fact that we have 55 pairs of twins with one only affected indicates that external factors are probably not responsible for the defects. Of the 55 cases, 15 did not give any data as to the sex of both twins, although 5 of the 15 cases were definitely stated to be binovular. In the 40 instances in which the sex of both twins was given, and but one was affected, there were 9 pairs of male twins, 10 pairs of female twins, and 21 pairs of mixed twins. This is a very close approximation to the 1:1 ratio of like-sexed to mixed twins expected in a group of binovular twins. As was stated above, if heredity is the explanation of malformations, then all twins should be of the binovular type when but one is affected. The data, furnished by the group with but one affected, support strongly the idea that heredity is the cause, and offer no support for the idea that an external factor such as barometric pressure is responsible for the malformations.

Let us look at the information yielded from the group of twins where *both are affected*. There were 33 such pairs of twins. In the case of one pair, both were affected, each had a different malformation, and the sex of the twins was not given. In the 32 instances in which sex was given, both twins had the same defect in every case. There were 15 pairs of male twins, 13 pairs of female twins, and 4 pairs of mixed twins. This is about a 4:3:1 ratio, due to the great predominance of the twins of like sex. Now it might be argued that in this group, barometric pressure was acting equally on both twins, and so this group would support the theory of Petersen. It does not support it however, due to the peculiar sex distribution among these twins. If barometric changes were the explanation, we should find the ratio of 1:1:1 that is found among twins in general. That ratio is altered, because we have concentrated in this group all the monovular twins where the sex must be the same in both, plus the binovular twins where the sex may or may not be the same.

We can determine with some accuracy by two methods how many of these twins should be monovular, and the two results should be in fair agreement. In the first group of twins there were 21 pairs of

mixed twins. Therefore there should have been 42 pairs of like-sexed twins, if this group was representative of twins in general. There were only 19 pairs of like-sexed twins, which meant that approximately 23 pairs of monovular twins were excluded from this group, and should be found as an excess in the group where both twins are affected. In the second group of twins, there were 4 pairs of mixed twins, and so there should have been 4 pairs of binovular twins of like sex, with both affected to correspond to these. There were actually 28 pairs of like-sexed twins, which gives us 24 pairs which were probably monovular. Thus from the first series we see that there should be 23 pairs of monovular twins in the second group, and analyzing the second group, we see that there should be approximately 24; an agreement so close as to be almost identical. Adding the two groups together we have 24 pairs of male twins to 23 pairs of female twins to 25 pairs of mixed twins, again an almost ideal approximation to the 1:1:1 ratio found among twins in general.

That the like-sexed twins are concentrated in the group where *both* are affected; and the ratio expected of males, females, and mixed pairs for binovular twins found where but one is affected, is very good evidence that the malformations in question are not determined by environmental causes but by inherited defects in the germ plasm.

One word must be said here as to joined twins and amorphous twins. Joined twins are necessarily of the same sex, and frequently the only malformation they exhibit is that brought about by their fusion. They were omitted, since they would have unduly weighted the group of twins with both malformed and both of the same sex. Amorphous twins, such as headless or bodyless twins, cases of acardiacus, etc., were omitted. When sex is distinguishable, such a twin and the normal twin are always of the same sex, the two having arisen through the division of a single fertilized zygote into two components, one with a complete set of determiners for normal development, the other with such an incomplete set of determiners as to prohibit development entirely, were it not for the collateral circulation from the normal twin which keeps the other shapeless mass alive. Here although we do have a normal child and an abnormal mass arising from the same egg, they cannot be added to this series, since the amorphous masses cannot properly be called an individual, but are incomplete fragments of human tissue, often without any trace of sex at all.

Incidence of Malformations in Several Siblings.—The evidence from the data furnished by the twins is in favor then of the interpretation that these malformations which we have been discussing, such as spina bifida, anencephaly, exomphalos, lack of arms or legs, atresia of the esophagus, duodenum, imperforate anus, etc., are hereditary. There is a second point which is in favor of this interpretation. If these defects

in development are hereditary, that is, are dependent upon factors resident in the germ plasm, then we should expect to find some families in which more than one child is affected, although we would expect the number of such families to be in the minority. The 1,420 cases were investigated from that standpoint. In 295 instances, the affected child was the first and only child in the family, hence there was no opportunity for a second one to be affected at the time the record was written. Of the remaining 1,125 cases, 311 had records of other children in the family showing a congenital malformation. This was an incidence of siblings affected in 27.6 per cent of the cases. There were 78 cases where 2 in the family were affected; 26 cases where 3 in the family were affected; 15 cases where 4 were defective; 1 where there were 5; and 2 where there were 6 malformed infants.

In the majority of instances, the type of malformation was the same in the affected siblings; in some it was different. Thus in 16 of the 78 families where 2 children were malformed, the type of malformation was different; in 62 families it was the same. In 6 families of the 26 where 3 were affected, the type of malformation was different; and in 20 it was the same. One out of 15 families where 4 were affected had 3 types of malformations, and 1 of the 2 families with 6 affected had different conditions affecting the various members. Sometimes the malformations which were listed as different were in reality due to the same process, but occurring in different sites in the body. Thus one child would have spina bifida in the lumbar region, while a second one in the family would have an encephalocele; or one child would show atresia of the duodenum, while another would be born with imperforate anus.

Petersen's idea concerning the effects of barometric pressure upon the products of conception could of course be put to experimental test. If the explanation holds good for human embryos, it should hold equally for animal embryos. Animals could be put into a sealed chamber in which the barometric pressure could be altered at will. The effect on the progeny could then be studied. Before such an experiment was carried out, however, every animal should be genetically controlled to see whether it produces malformations spontaneously. Thus each male and each female should be bred several times to an unrelated mate, and several times to a related mate, and records carefully kept of all the relationships and the results. Then unrelated males and females, who even when bred with their own litter mates, have produced no malformations, should be bred under the altered barometric pressures, and under normal conditions. Should the number of malformations be considerably greater under the altered pressures, when the same parents show no malformed offspring under normal pressures, we might be led to conclude that altered pressure at the time of conception was a predisposing factor to the production of malformations. Experiments which are de-

signed to test this or other ideas, such as malformations caused by unbalanced diets, etc., are worthless unless the genetic aspect of the experiment is rigidly controlled.

It is true that malformations can be produced experimentally in forms like fish by altering the temperature, the chemical constitution of the environment, the oxygen available, and that one cannot claim that such malformations are inherited in these forms. One might as well argue, however, that because one can produce diabetes by removing the pancreas, that all cases of diabetes are due to a complete absence of the pancreas. It is true that one can produce malformations in the mammalian forms by irradiation of the ovary before conception takes place, but no one would be rash enough to claim that malformations which have been known since the beginning of man's history have been due to irradiated ovaries. Moreover, such malformations as Bagg¹ has produced by this method have been shown to be due to a disturbance of the chromosomes by the irradiation, and hence of the hereditary constitution of the animal, for without further experimentation these malformed mice, which have been produced through irradiation of the egg from which they came, have passed on the defect through numerous generations of their descendants.

SUMMARY

A group of 1,420 cases of congenital malformations, either evident externally, or shown by operation or autopsy, were investigated. Of these, 256 gave either the date of the last period, or the birth date of the child, with a statement as to the duration of pregnancy, from which data the month of the conception could be determined with fair accuracy. No significance could be attached in this series to the possible barometric disturbances as a possible cause of malformations.

In the 1,420 cases of malformations were found 40 cases of twins, with one twin malformed; and 32 cases of twins where both twins were malformed, and the sex of the twins was mentioned. The sex distribution in these two groups of twins showed that there was a concentration of binovular twins whose heredity need not be identical, in the "one-twin-malformed group." There was a concentration of like-sexed twins, most of them monovular in the "two-twins-malformed" group. This strongly suggests that hereditary causes are responsible for congenital malformations.

In this group of 1,420 cases, there were 1,125 which occurred in families which had more than one child. There were 311 cases, or 27.6 per cent of these, which were in families where two or more children were malformed. In 60 of the 311 cases, the malformations were not identical in the various members of the family; in the remaining 251 or 80 per cent of the cases, the malformations were identical. This again strongly suggests that the malformation is hereditary in nature. When

there is such a wide variety of malformations to be exhibited, the fact that in 80 per cent of the cases where two or more are malformed in the family, the type of defect is the same in the different affected members, indicates some cause more deep seated than chance variation in barometric pressure.

Inherent defects in the determiners for development are responsible for the vast majority of congenital malformations in man.

I wish to express my appreciation to Dr. Charles C. Macklin, who suggested this study, for his continued support of my studies on the rôle of inheritance in the etiology of disease.

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INTRATHECAL INJECTION OF A SOLUTION OF ALCOHOL FOR INTRACTABLE PAIN IN THE PELVIS AND LOWER EXTREMITIES

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THE problem of controlling pain in inoperable malignancies has always been discouraging and because of our helplessness these unfortunate patients are greatly neglected.

It is the purpose of this report to record a method for the relief of intractable pain in the pelvis and lower extremities, and to present the results of its use in ten cases of pelvic carcinoma with involvement of the lumbosacral plexus. The method although not original in the main is somewhat of a departure from that used by others.

TECHNIC

With the patient lying on the least affected side, a spinal puncture needle is introduced in the usual manner between the second and third lumbar vertebrae. Ten cubic centimeters of spinal fluid is withdrawn and discarded. Ten cubic centimeters of a 5 to 7.5 per cent solution of sterile absolute alcohol and triple distilled water is then injected rather rapidly into the spinal canal. The patient is immediately placed flat on the back and required to remain in that position for four hours.

The materials required for the injection are the following: Three medicine glasses; two 10 c.c. syringes; a tuberculin syringe; a 2 c.c. syringe and a hypodermic needle; a small gauge spinal puncture needle with a short bevel; 0.5 to 0.75 c.c. of a sterile absolute alcohol; 9.5 c.c. of sterile triple distilled water; and one small ampule of 1 per cent novocaine.

In this series, eight cases of carcinoma of the cervix, one case of carcinoma of the vulva, and one case of carcinoma of the ovary were

treated. All of these patients were on the cancer service of Dr. Cameron Duncan in Kings County Hospital, Brooklyn, New York, and this work was made possible through his kind cooperation. Brief details of these cases are given as an example of the results obtained.

CASE 1.—E. B., aged forty-five, was admitted to Kings County Hospital, with a diagnosis of carcinoma of the cervix with metastases to the spine. During the past eighteen months she had received extensive x-ray and radium therapy. Two months preceding admission a bilateral cordotomy was performed. She was fairly comfortable for one month, following which there was a return of the old type of pain. On admission she complained of severe pain in the abdomen and back radiating down the legs. The left leg was swollen and the patient was generally in poor condition. After using large and frequent doses of morphine for one month the pain could not be controlled. On Dec, 9, 1933, she was given 10 c.c. of a 5 per cent solution of alcohol according to the technic described above. Thirty minutes later the pain in the pelvis and legs was markedly diminished. She complained of a slight weakness in both legs. This was scarcely appreciable since she had weakness and swelling in both legs before the injection. Analgesia was present in both legs and thighs. Slight hyperesthesia was present over both thighs. There was no bladder or rectal incontinence. From that day until the time of her death, three months later, she was almost entirely free from pain in the lower abdomen and legs. The only sedatives that were necessary following the injection were occasional doses of acetyl-salicylic acid and codeine.

CASE 2.—S. H., aged thirty-seven, was admitted to the hospital with a diagnosis of carcinoma of the cervix with widespread pelvic extension. X-ray and radium therapy were instituted shortly after admission. This patient suffered from a great deal of pain in the abdomen and lower extremities, but was still ambulatory. Little palliation of pain was obtained following irradiation. Occasional doses of morphine with mild sedatives were used unsuccessfully for relief. Ten cubic centimeters of a 5 per cent solution of alcohol were injected intrathecally. Two days after the injection this patient had obtained excellent relief of pain, and it was never necessary during the next four and one-half months, until her death, to give her more than an occasional dose of acetyl-salicylic acid and codeine. Immediately following the injection she suffered a very severe headache which lasted for about twelve hours. Slight weakness in the lower extremities was present with diminished patellar reflexes. Hyperesthesia was present as high as the distribution of the ilio-inguinal nerve. There was no bladder or rectal sphincter disturbance. The patient was up and around on the second day after the injection.

CASE 3.—J. K., aged forty, was readmitted to the hospital after having received extensive x-ray and radium therapy on previous admissions. Diagnosis of carcinoma of the cervix with wide extension and metastases to neighboring lymph nodes. The patient was still ambulatory although pain on motion was excruciating. Frequent doses of morphine were necessary for relief. Intrathecal injection with 5 per cent solution of alcohol was done. Maximum relief was obtained on the third day. Only a dull pelvic and lower extremity pain were complained of from that time until her death two months later. Morphine was gradually diminished and she was finally kept comfortable with acetyl-salicylic acid and codeine. Shortly after the injection tendon reflexes were diminished. There was slight motor weakness of the lower extremities with hyperesthesia extending to four fingers above the pubis. Bladder and rectal sphincter action remained normal. This patient continued to be ambulatory until shortly before her death two months later.

CASE 4.—M. W., aged thirty-five, who had received a complete course of x-ray and radium therapy during a previous stay in this hospital, was readmitted. Diagnosis on the first admission was that of a carcinoma of the cervix with extension through the pelvis and metastases to the surrounding lymph nodes. The condition had not appreciably regressed at the time of this admission. She was complaining of intense pain in the abdomen and legs. Since this was one of our first cases, she was given an intraspinal injection of 10 c.c. of only a 2 per cent solution of alcohol. She obtained no relief of pain. Clinically there were no signs of diminished motor function, hyperesthesia, or sphincter disturbances. This patient refused a second injection and the therapy was a failure due to inadequate dosage.

CASE 5.—J. L., aged sixty-three, diagnosis of carcinoma of the vulva with metastases to both inguinal lymph nodes. This patient on a previous admission to the hospital, about eight months ago, had been subjected to an operation for complete vulvectomy. Since the lesion was small, removal of the inguinal lymph nodes was not done, but she received a full course of irradiation over these glands. On her present admission inguinal glands on both sides had become extensively involved. Glands in the left inguinal region had broken down with deep slough down to the femoral vessels. This patient was bedridden and pitiful in her misery. She was given 10 c.c. of a 5 per cent solution of alcohol intrathecally. By the third day she had obtained good analgesia in the lower abdomen and lower extremities. As in all of our cases the patellar reflexes were diminished, and she had slight motor weakness of the lower extremities for about twenty-four hours. Hyperesthesia extended to about the level of the distribution of the eleventh thoracic nerve. This patient had a very violent headache which persisted for eighteen hours and could only be relieved with morphine. Bladder and rectal sphincter action remained normal. Pyramidon and codeine were sufficient to keep her comfortable up to a few days before her death, four and one-half months later, which followed erosion through the femoral vein.

CASE 6.—K. A., aged thirty-four, admitted to the hospital with an advanced carcinoma of the cervix with wide parametrial extension and pelvic metastases. X-ray was begun for palliation. Since her pain was so intense, she was given 10 c.c. of a 5 per cent solution of alcohol intraspinally, and by the fourth day had obtained excellent relief of pain. She showed diminished reflexes and slight weakness. Moderate hyperesthesia was present as high as the level inguinal ligaments. There was no disturbance of the bladder and rectal sphincter action. Relief continued until her death six weeks later.

CASE 7.—N. C., aged thirty-two, admitted to the hospital with a diagnosis of a carcinoma of the cervix with extension into the bases of both broad ligaments, but no evidence of other metastases. Intraspinal injection of 10 c.c. of a 5 per cent solution of alcohol was done, and on the second day, she had obtained good relief of pain. Hyperesthesia, motor weakness, and diminished tendon reflexes in the lower extremities were all present for about twenty-four hours. Bladder and rectal sphincter action continued to be normal. Radium followed by x-ray treatment were instituted. Until her death three and one-half months later, following exsanguinating hemorrhages, she was kept comfortable with acetyl-salicylic acid and codeine.

CASE 8.—C. L., aged forty-four, admitted to the hospital with a diagnosis of carcinoma of the cervix with involvement of the entire pelvis. Patient was in an extremely weakened condition and suffering from unbearable pain. Ten cubic centimeters of a 5 per cent solution of alcohol were given intrathecally. The maximum effect was evident by the second day and good relief of pain was obtained. Motor

weakness and hyperesthesia in both lower extremities with lessened reflex responses were noted. Bladder and rectal sphincter action remained normal. Acetyl-salicylic acid and codeine were all that was necessary to keep her comfortable during the following month. At that time she developed a psychosis and became so violent that it was necessary to administer additional sedatives and to keep her in a strait-jacket until death one month later.

CASE 9.—E. T., aged seventy, admitted with carcinoma of the uterus thought to have originated in the fundus, but now so widespread throughout the pelvis and lower abdomen that the original focus could not be definitely determined. She had received an unknown amount of x-ray therapy about two years previous to admission. This patient was ambulatory and was suffering a great deal from pain in her lower abdomen and legs. She was given 10 c.c. of a 7.5 per cent solution of alcohol intrathecally. By the third day after the injection she had obtained good relief of her pain. No change in the function of her bladder and rectal sphincter was noted. She continued to be ambulatory although for the first twenty-four hours she complained of slight weakness in her legs. Patellar reflexes were diminished. Hyperesthesia was rather marked, and she complained of a sensation of tingling in her lower extremities. She was kept comfortable with pyramidon and codeine until the time of her death two months later.

CASE 10.—C. K., aged fifty-five, admitted to the hospital with a diagnosis of carcinoma of the ovary with generalized abdominal metastases. The patient had had exploratory laparotomy two months previous to this admission, followed by deep x-ray therapy. She was suffering from exquisite pain in the lower abdomen and was unable to obtain any rest. Ten cubic centimeters of a 7.5 per cent alcohol solution was given intrathecally. Examination showed lessened reflexes, moderate motor weakness, and mild hyperesthesia of the lower extremities. There were no bladder or rectal disturbances. Acetyl-salicylic acid and codeine were sufficient for relief of pain until her death one week later.

REVIEW OF LITERATURE

In 1931 Dogliotti¹ reported the first series of more than 40 cases in which alcohol had been given intraspinaly for the relief of pain in the lower extremities. In his series he used 0.5 to 1 c.c. of absolute alcohol (undiluted). His needle was inserted between the second and third lumbar vertebrae, and the patient was made to lie on the unaffected side for twenty minutes following the injection. It is interesting to note that he dared to use this therapy in sciaticas, radiculitis, in arthritis deformans, tabetics, femoro-cutaneous neuralgias, perineo-eccecygeous pain, intercostal neuralgias, and diabetic neuritis. He suggested at the time the possibilities of its use in pelvic malignancies. Some time later when he was visiting F. C. Yeomans Clinic, he was invited to demonstrate his method on a patient with inoperable carcinoma of the rectum. Subsequently Yeomans² reported a series of seven similar cases all with good results. In the past year, Saltzstein,³ using the method of Dogliotti has reported good results in the relief of pain. His cases included 1 case of carcinoma of the breast, 1 case of carcinoma of the prostate, and 5 cases of carcinoma of the cervix. At about the same time, Stern⁴ reported a series of 19 cases of carcinomas, in the majority of which he considered having obtained satisfactory results by the use of Dogliotti's method. Stern gave injections as high as the seventh thoracic interspace, and suggested injections as high as the first thoracic interspace. More recently Greenhill and Schmitz⁵ have reported an additional series of 25 patients all with malignancies of the female genital organs. They obtained relief in 24 of the 25 patients treated.

Opinion differs as to the length of time required to get the maximum effect from the drug. Dogliotti reports some cases as taking as long as ten to twenty days. Saltzstein says relief was immediate in all of his cases. Stern, Greenhill, and Schmitz coincide in their findings with Dogliotti. Examination of the patients in this series showed greatest relief on the fourth day after injection.

Reactions are not disturbing. Headaches occur in about 50 per cent of the cases. The incidence may be diminished by forcing the patients to lie flat on their backs for the full four hours. In two cases the headache persisted for twenty-four hours, and sedatives were required for relief. Tendon reflexes are diminished and a slight transient motor weakness, lasting from one to four days, is usually present. Hyperesthesias can be elicited, both superficial and deep, up to the level to which the analgesia has extended. In only one case was this sufficiently marked to cause the patient to complain of pain from the bedclothes touching. This hypersensitivity had disappeared by the second day. Bladder or rectal sphincter disturbance did not occur in any case.

In one case of Dogliotti's series there was retention of urine for forty-eight hours followed by the return of normal sphincter action. Greenhill and Schmitz report one case in which 2 c.c. of absolute alcohol injected intraspinaly within a period of two days caused atrophy and anesthesia of the left leg. Stern reports a case in which 30 minims of absolute alcohol caused complete loss of muscle, tendon, and joint sense, and loss of control of the lower limbs, and a second case in which an injection of sixteen minims of absolute alcohol caused sensory bladder paralysis for one week.

Sicard and Byrne¹² believe that sensory fibers are more susceptible to the effect of alcohol than are the motor fibers. Cadwalader claims that both were affected alike. I tend to agree with the latter view.

Since no patient in this series lived longer than four and one-half months, it is impossible to say how much longer the analgesia would have lasted. Other patients reported were kept comfortable for from six to eighteen months.^{1, 2} The results to date make this type of treatment appear to be the most efficacious of the many methods that have been tried, and its technic is sufficiently simple to promote its widespread use and determine its true value in a large number of cases.

Brief mention is made of the other methods in use at the present time for the relief of pain in these cases, merely in order to contrast them with this type of therapy. We may divide them into two groups, those in which sedatives are used to dull the appreciation of pain and those in which there is an actual interruption of the nerve pathways either by surgery or by degenerating drugs.

The use of sedatives, principally the opiates, are seldom satisfactory since the increasing tolerance of the patient for the drug makes larger and larger doses finally inadequate for the control of the pain. Frequently we must forego the use of opiates entirely because of disturbing idiosyncrasies to opium derivatives.

In the surgical interruption of the nerve tracts a rhizotomy, peripheral nerve section, cordotomy, or sympathectomy may be performed. However, specialized technic is necessary in these procedures, and they are all attended with some shock in patients who are not considered good operative risks.

In the use of degenerating solutions for destruction of the nerve pathways the more usual operations are paravertebral injections of the peripheral nerves, sacral epidural injections and occasionally attempts are made to do paravertebral injection of the sympathetic ganglia. Failure is much more frequent than is success in these cases because of the difficulty of locating these nerve tissues through four or five inches of muscle and fat. If the injection of a peripheral nerve is correctly done, transmission of all motor and sensory impulses are destroyed. If the area to be relieved of pain is large, this complete anesthesia and motor paralysis will be very disturbing.

COMMENTS AND CONCLUSIONS

1. Although no marked motor or sensory disturbances have been encountered in this series this treatment seems, at present, too radical to recommend in any but incurable cases.

2. Injections in this series were made in the second lumbar interspace or lower. In this region there is no cord, but only cauda equina, and we are also below the extent of the dorsal suspensory ligament of the cord which is believed to prevent free passage of fluid from one side of the spinal canal to the other, but this has never been proved. Injections are made rapidly for the purpose of equal and widespread diffusion of the alcohol solution over the lumbar nerve roots and cauda equina, usually bilateral relief is desired, and this is the method of obtaining it. Alcohol in the spinal canal, even if not barbotaged, diffuses fairly rapidly. Torsion of the spinal canal is not considered necessary in the solution injection method. The analgesia is similar to that produced by small doses of well-barbotaged spinal anesthetic drugs, but since the nerve narcosis with alcohol is more persistent, it is better suited for our purpose.

3. A great deal of pain in the abdomen and lower extremities from pelvic carcinoma is reflex. The wide distribution of the pain with proof of the absence, in many cases, of direct pressure on peripheral roots and trunks, suggests involvement by irritation of the cord segments from which these nerves arise. It is found that the termination in the cord of the sympathetic and sacral autonomic fibers from the diseased area corresponds to the segments of origin of the peripheral nerves involved in the distribution of pain. It is thought that the sympathetic and sacral autonomic fibers making up the hypogastric plexus are not paralyzed by this strength of solution but their conductivity is greatly reduced. The fact that occasional bladder and rectal disturbances are reported favors the belief that a large amount of the benefit derived from this therapy is by its effect on the autonomic nervous system. There is some direct effect on peripheral nerves, since we get hyperesthesias and motor weakness in all areas supplied by the peripheral nerves in the region of injection. Immediate relief of pain is probably due to the direct effect on

peripheral nerve roots, later progressive relief of pain up to the fourth day is due to gradual recovery of the irritated cord segments following diminution of the steady stream of stimuli through the sympathetic and sacral autonomic afferent fibers.

4. A low concentration of alcohol is sufficient to diminish the conductivity of the nerve fibers so that only strong, and repeated impulses will pass through. An initial dose of 10 c.c. of a 5 per cent to 7.5 per cent solution repeated once after four days is considered within the limits of safety.

5. Pain was markedly diminished in all cases except one. In the failure, only a 2 per cent solution was used, which is an inadequate dose, and the patient refused a second injection. The results obtained in this series would indicate that this type of treatment is more successful in selected cases than is paravertebral injection of spinal nerves and sympathetic ganglia, sacral blocks, and occasionally even cordotomy. Complete anesthesia cannot be expected but there is always excellent analgesia. Peripheral pain was poorly relieved in areas supplied by nerve roots originating in the spinal cord above the twelfth thoracic and first lumbar segments.

6. Dogliotti's method seems preferable in cases of unilateral localized involvement and where pain is due to direct pressure on the peripheral nerve trunk.

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MEDICAL ARTS BUILDING

Roberto, S.: The Presence of Vitamin E in the Blood of Fertile Women, Riv. ital. di ginec. 18: 105, 1935.

The author, after thorough discussion of the question of vitamin E, refers to the results of his experimental research on the presence of this vitamin in the blood of fertile women. Using the rat for the experiments he states that while the function of reproduction is profoundly impeded in animals placed on a synthetic diet lacking the E factor, it persists unchanged in those in which is administered the same diet with the addition of blood from pregnant women.

In conclusion he infers that in the blood of fertile women there is present a rich source of the E factor.

AUGUST F. DARÓ.

A STUDY OF THE ACTION OF THE GONADOTROPIC SUBSTANCES PRECIPITATED BY TANNIC ACID

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THE early determination of pregnancy by subjective physical changes and the objective findings is rather unreliable. However, the determination of pregnancy by chemical reactions is relatively much more accurate. Such chemical reactions may be demonstrated by: *first*, color changes;¹⁻³ *second*, pupillary reactions;⁴ or, *third*, the ovarian reaction to the stimulating substance present in body fluids during pregnancy. These ovary-stimulating substances have been reported to be present in the blood, urine, placenta,⁵⁻⁷ decidua, colostrum,⁸ amniotic fluid, and saliva^{9, 10} of pregnant women and in milk^{8, 11, 12} and the serum of blisters produced by cantharides.¹¹ They are said to be absent in cerebrospinal fluid¹³⁻¹⁶ and gastric juice^{9, 15} of pregnant women. In the human, the placenta, blood serum, and urine contain the substance or substances in greatest amounts. The precipitants which have been used either on crude urine or on a partially purified product have included not only such solvents as alcohol and acetone¹⁷⁻¹⁹ but also the following: 1. kieselguhr,²⁰ 2. ammonium sulphate,²¹ 3. tannic acid,²¹ 4. phosphotungstic acid,^{22, 23} 5. Lloyd's reagent,^{11, 24} 6. kaolin,²⁵ 7. norit,^{19, 26, 27} 8. benzoic acid,²⁷ 9. tungstic acid,^{28, 29} 10. uranyl acetate,³⁰ 11. aluminum hydroxide,³¹ 12. phosphomolybdic acid,²³ 13. sodium tungstate,³ 14. colloidal iron,^{21, 22} 15. alundum,³¹ 16. tricalcium phosphate,³¹ and 17. talc.³¹

Tannic acid has never been used on crude urine.* Dickens²¹ tried it on a partially purified solution of the ammonium sulphate precipitate of pregnancy urine and reported that "it caused nearly quantitative precipitation of the activity." We believe that because of its comparative cheapness, tannic acid would serve well in the preparation of the gonadotropic substance from crude urine and other secretions of the body. We have studied its use for this purpose both in urine and in saliva.

EXPERIMENTAL

Urine from women pregnant five to seven months, obtained from the Out-Patient Department of the University Hospital, is acidified to a pH 4 to 5 (spot plate method) with glacial acetic acid, using bromocresol green as the indicator. If the

*After we had completed our work we learned that Hellbaum, Fevold, and Hilsaw had reported on the use of tannic acid to concentrate the gonadotropic activity in crude urine in *Proc. Soc. Exper. Biol. & Med.*, p. 1566, June, 1935.

The author wishes to express his appreciation for valuable suggestions given by Dr. J. B. Goldsmith, of the Department of Histology and Embryology, and Dr. Edward C. Mason, of the Department of Physiology.



Fig. 1.—Ovary of immature rabbit receiving intravenously (in four equally divided doses at fifteen-minute intervals) the substance precipitated from 240 c.c. of pregnancy urine.



Fig. 2.—Ovary of a mature rabbit killed twenty-two hours after receiving an ammoniacal solution of the substance precipitated by tannic acid from 125 c.c. of urine of pregnancy.

urine is not clear after acidifying, it is centrifuged. One per cent by weight of tannic acid, dissolved in the least amount of water, is added. The heavy gray white precipitate may be centrifuged immediately or stand in the ice box overnight or longer. It is then centrifuged, washed with alcohol and ether, and extracted immediately with a small amount of approximately tenth-normal ammonium hydroxide, or permitted to stand under an alcohol-ether mixture overnight (or longer) and extracted the next day. It was observed that our immature rabbits did not survive the injection of an extract prepared from 25 c.c. or more of pregnancy urine, whereas mature rabbits survived the equivalent of 125 c.c. or more. The earliest changes in immature female rabbits were observed four hours after injection, and consisted of hyperemia of the uterine horns and tubes, injection and interstitial hemorrhage of the ovaries, and degenerative follicular changes. Fig. 1 is a photomicrograph of a paraffin section of the ovary of an immature rabbit, dying four hours after receiving the first of four injections (given at fifteen-minute intervals) of the substance precipitated from 240 c.c. of the urine of pregnancy. It illustrates the changes mentioned above.

Our findings are contrary to the observations of Reinhart and Scott²² who state that "luteinization of the hemorrhagic follicles in the rabbit ovary begins between the forty-eighth and ninety-sixth hour after injection; and there are then seen partially luteinized hemorrhagic follicles." We found microscopic evidence of luteinization in our mature rabbits which had received the substance precipitated by tannic acid at nineteen to twenty-two hours after the injection; and gross evidence of luteinization and hemorrhage at the end of thirty-six hours. Fig. 2 is a photomicrograph of a paraffin section of the ovary of a mature rabbit killed twenty-two hours after receiving an ammoniacal solution of the substance precipitated by tannic acid from 125 c.c. of urine of pregnancy.

To determine whether 1 per cent by weight of tannic acid was sufficient to insure complete precipitation, the supernatant liquid was tested with more tannic acid. No further precipitation occurred. Furthermore, a white mature female rabbit which received an intravenous injection of 10 c.c. of the supernatant urine showed no gross indication of the pregnancy hormones.

EFFECT OF INTRAVENOUS INJECTION OF THE ALCOHOL-INSOLUBLE FRACTION OF THE AMMONIACAL SOLUTION

The addition of 20 to 30 volumes of 95 per cent ethyl alcohol to each volume of the ammonium hydroxide solution of the substances precipitated by tannic acid from the urine of pregnant women precipitates a dirty white, flocculent, active substance which is soluble in water. Fig. 3 is a photomicrograph of a paraffin section of the ovary of a mature rabbit killed forty-two hours after receiving intravenous injections of an aqueous solution of the substance precipitated by alcohol, from an ammoniacal solution of the active substance obtained from 285 c.c. of urine by precipitation with tannic acid. It shows hemorrhage in a luteinized follicle. Fig. 4 is a photograph of a longitudinal section of the ovary of a mature rabbit killed nineteen hours after receiving an intravenous injection of the alcohol-insoluble fraction (two precipitations) of the ammoniacal solution of the active substance from 68 c.c. of urine. The lutein bodies are very prominent.

Our observations are contrary to those of Elden²³ who states, "The active material, after adsorption and extraction from urine of pregnancy, is not precipitated by alcohol, acetone, or ammonium sulphate"; and Wiesner and Marshall²² who state, "No active precipitate has been obtained (in two experiments) from an ammoniacal solution of the active substance by the addition of alcohol to a concentration of 90 per cent." A biuret test, made on an aqueous solution of the active substance, prepared as described is negative.¹⁷

It was observed that an immature rabbit did not survive the injection of material obtained, as described, from more than 135 c.c. of urine of pregnancy; whereas, a mature rabbit tolerated 285 c.c., or more. The earliest gross changes in the mature female rabbit were present at nineteen hours and consisted of the formation of corpora lutea. Later changes included hemorrhage into the luteinizing follicle. This harmonizes with the statements concerning luteinization and hemorrhage in the rabbit, found in Maximow and Bloom *Text-Book of Histology*, second edition.



Fig. 3.—Ovary of a mature rabbit killed forty-two hours after intravenous injections of the aqueous solution of the substance precipitated by alcohol, from an ammoniacal solution of the active substance obtained from 285 c.c. of pregnancy urine.



Fig. 4.—Ovary of a mature rabbit killed nineteen hours after receiving intravenously the alcohol insoluble fraction of the ammoniacal solution of the active substance obtained from 68 c.c. of pregnancy urine.

The earliest changes in immature female rabbits were observed three and one-fourth hours after injection and consisted of hyperemia of the uterine horns and tubes, enlargement, injection, and interstitial hemorrhage of the ovaries. Microscopic examination of the liver and kidneys of animals receiving this injection revealed marked changes at the end of seventy-two hours. Dr. L. A. Turley, of the Department of Pathology, points out that in the frozen section of the kidney the

capillaries of the glomeruli are swollen. The tubules contain albuminous debris and the tubule cells show degenerative changes. There are present a few red blood cells, both in the tubules and in the subcapsular space of the glomeruli. Also, in the frozen section, the liver cells show marked degenerative changes. There are a few areas of hemorrhage. The epithelial lining of the bile ducts is swollen. These changes are at present receiving further consideration in our laboratory.

EFFECT OF ORAL ADMINISTRATION

The effect of the enzymes upon the gonad-stimulating substance was studied by Dickens²¹ who stated that it "is not rapidly destroyed by trypsin or pepsin though prolonged treatment causes inactivation"; and by Wiesner and Marshall²² who state definitely that the activity is destroyed by trypsin. The oral administration of the gonadotropic substance has been tried on rats^{20, 24} with a variable degree of success.

We administered the extract obtained from 200 c.c. of human pregnancy urine by tannic acid precipitation, extraction with dilute ammonium hydroxide, and reprecipitation with 25 volumes of 95 per cent ethyl alcohol, in an aqueous solution via stomach tube, and seventy-two hours later both gross and microscopic findings were negative for pregnancy.

EFFECT OF INJECTING WHOLE SALIVA INTRAVENOUSLY

Contradictory statements are found concerning the presence of the hormones in saliva. Traneu-Ranier,⁹ working with infantile mice, obtained follicle ripening but stated that hemorrhage into the follicle is very weak and seldom seen; and typical lutein bodies are rare. Ofstad,¹⁰ also working with mice, found no gross or microscopic evidence of the presence of the hormones. At the suggestion of Dr. Edward C. Mason, of this department, we have studied the action of the saliva of pregnant women on both mature and immature female rabbits. In one mature rabbit, isolated three months, which received 18 c.c. of saliva intravenously at 3:00 P.M. and was found dead the next morning, we observed microscopically two well-formed corpora lutea. In immature rabbits receiving injections of saliva, no lutein tissue was observed. There were, at the end of thirty-six hours, however, degenerative changes of the granulosa, small amounts of hemorrhage into a few follicles, and an injection of all the vessels. In one immature animal the uterine horns and tubes were injected sixty hours after the initial intravenous injection. All animals, regardless of their age, showed a strong shocklike reaction to the intravenous injection of untreated saliva. Experiments attempting to determine the cause of this condition are being conducted at the present time.

Fig. 5 is a photomicrograph of a paraffin section of the ovary of an immature rabbit, forty-nine hours after the first injection of saliva of a pregnant woman. It shows degenerative changes and hemorrhage in the follicle.

EFFECT OF INTRAVENOUS INJECTION OF THE AMMONIACAL SOLUTION OF THE TANNIC ACID PRECIPITATE OF SALIVA OF PREGNANCY

One mature rabbit which received the extract made from 25 c.c. of saliva showed no positive gross findings at the end of forty-six hours. Microscopically, we observed some indefinite changes of the granulosa and numerous red blood cells in the coagulum of the follicles. In two immature rabbits which received the extracts made from 45 c.c. and 110 c.c., respectively, there were no gross changes at the end of twenty-six and sixty-seven hours; but microscopically, we observed injection

(especially of the thecal vessels), degenerative changes of the granulosa layers and an infiltration of leucocytes and red blood cells into some follicles. Fig. 6 is a

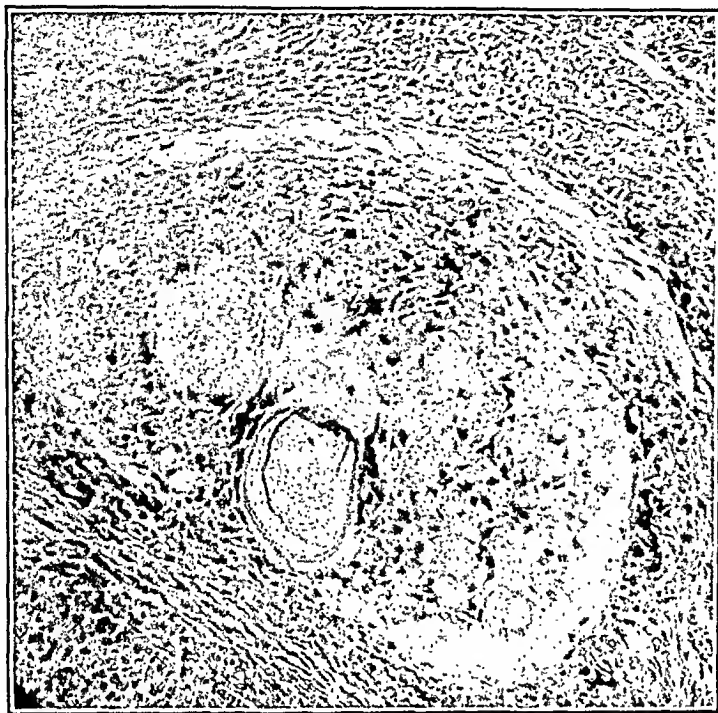


Fig. 5.—Ovary of immature rabbit forty-nine hours after the first injection (of a series totalling 53 c.c.) of whole saliva of pregnant women.



Fig. 6.—Ovary of immature rabbit sixty-seven hours after receiving intravenously the ammoniacal solution of the substance precipitated by tannic acid from 110 c.c. of saliva of pregnant women.

photomicrograph of a paraffin section of the ovary of a rabbit sixty-seven hours after receiving the ammoniacal solution of the substance precipitated from 110 c.c. of saliva of pregnant women, by tannic acid.

DISCUSSION

The difference in the response of mature and immature rabbits both to saliva and to urine indicates the greater sensitivity of the mature animals. It is conceivable that some of the contradictory observations on saliva are due to this fact. The occasional false negative reactions, using urine, may be caused by the use of immature animals; or, at least, insufficient dosage for the immature animal.

King³⁵ who has made an analysis of 4,515 cases presented by thirty-four authors and involving seven different techniques, with minor variations, reports an uncorrected error of 3.9 per cent; of this, 3.3 per cent represent false negatives. Since most of the animals used in these techniques were immature, it is conceivable that the large percentage of false negatives may be partially, at least, due to the age factor. Wilson and Corner³⁶ advocate the use of fully matured female rabbits. They examine the animals sixteen hours after the injection, and their results compare very favorably with the results of other investigators who use immature rabbits but make the examination thirty-six hours after injection. Friedman,³⁹ in 1929, recommended mature rabbits. Hirsch-Hoffmann,³⁷ as well as Sar-louis,³⁸ advocate the use of mature mice.

CONCLUSIONS

1. Tannic acid completely precipitates a gonadotropic substance from crude urine, as evidenced by tests on mature and immature female rabbits. The substance obtained from as little as 15 c.c. of urine gives a strong grossly positive reaction at seventy-two hours in an immature female rabbit. The earliest conclusive change was observed twenty-two hours after injection.

2. Alcohol precipitates an active fraction from the ammoniacal solution. This precipitate produced gross luteinization nineteen hours after injection in a mature rabbit.

3. The earliest postmortem findings were injection of the uterine horns and tubes, and swelling of the ovaries. These findings, however, were not constant.

4. Except for hyperemia and interstitial hemorrhage, the earliest ovarian changes noted were luteinization.

5. Oral administration was ineffective in the dosage given.

6. Crude saliva gave a positive microscopic test in one mature rabbit. No positive gross reactions were noted. Microscopic changes were observed in immature rabbits which received either crude saliva or an extract prepared by tannic acid precipitation; but these changes were not conclusive.

7. The amount of interstitial gland present depends upon the age of the rabbit.

8. Mature rabbits are more sensitive to gonadotropic substances than immature, a finding which agrees with that of other workers.

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Little attention has been paid to disturbances in the cardiovascular system as a cause of death in the toxemias of pregnancy. However, the electrocardiographic studies of Young have demonstrated that myocardial damage can be detected if systematic examinations are made many months after patients have had eclampsia. Winckler has observed acute cardiac failure in seven cases of preeclampsia during the past year and a half. In view of the fact that chloroform and chloral can produce harm to the cardiovascular system, Winckler is surprised that little mention is made of cardiac deaths during the course of the Stroganoff treatment of eclampsia.

For cases of preeclampsia he suggests a salt-free and protein-free diet. For the treatment of eclampsia he recommends immediate delivery. If operative interference in the form of a forceps delivery or a cesarean section is performed he employs a combination of chlorethyl-ether anesthesia. If convulsions occur after delivery, the author suggests that pernocton should be given in place of the chloroform-chloral hydrate routine recommended by Stroganoff. This will avoid damage to the heart.

J. P. GREENHILL

THE USE OF PITUITRIN INTRAVENOUSLY IN THE THIRD STAGE OF LABOR

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SINCE the introduction of pituitrin in obstetrics by Blair-Bell in 1909, no other drug has been exploited so extensively in this field of medicine. Each wave of enthusiasm has been followed by a similar period of adverse criticism, when many of the salient facts regarding its use were disregarded. During the past few years the intravenous use of pituitrin has again become prevalent; it may be well at this time to review its development.

In 1910 Foges and Hofstätter used pituitrin intravenously in two cases and observed that its action was quicker and more pronounced than when injected intramuscularly. It remained, however, for Hofbauer to discover the value of the drug in the treatment of postpartum hemorrhage, although in his original work he used it in the first and second stages of labor. He observed that the tetanic contractions usually occurred within a few seconds, but assumed a more normal course after several minutes had elapsed. In one of his papers, published in 1912, Hofbauer described the symptoms of what we now call pituitrin reaction. He often observed "pallor or slight cyanosis of the face, sweating, feeling of uneasiness or apprehension and apathy of the patient in labor." He furthermore reported satisfactory results in cesarean sections.

Continuing the work of Hofbauer, Sachs in 1914 and later in 1917, observed excellent results with this form of therapy during the third stage of labor, particularly in 12 cases of atony of the uterus. He was the first to suggest that hypertension might be a contraindication of its use, and in view of the criticism that marked relaxation followed the strong contractions, Sachs recommended that ergot be given before the action of pituitrin wore off. In spite of the fact that pituitrin was used intravenously both before and after the expression of the placenta, he noticed no ill effects. In fact, in 1917, he concluded that there was no other method which gave so prompt and sure an action as intravenous pituitrin.

The continued use of intravenous pituitrin met considerable opposition on the basis of animal experimentations and the strong influence of Stoeckel who, in 1925, objected to its routine use because of the supposed relaxation following its specific action. However, in 1926 Zorn recommended the use of this drug not only in the diagnosis of late ectopic pregnancy but also in outlining myomatous nodules in the pregnant uterus. Moreover, he employed it as an aid in teaching palpation to students, and suggested its use in ruptured uteri to control the bleeding from the smaller vessels. He never observed a case of incarcerated placenta.

In this country the use of pituitrin has been restricted to the third stage, mostly through the influence of the late J. Whitridge Williams. At the suggestion of Hofbauer, pituitrin has been used intravenously with good results since 1926 in Dr. Williams' clinic at the Johns Hopkins Hospital. Its use, however, has been limited to the period following the expression of the placenta.

Alden reported its use in the Boston Lying-In Hospital in 1933. He observed that the incidence of pituitrin reaction was greater when the patient had received pituitrin intramuscularly prior to the injection intravenously. Both he and Jackson, who discussed his paper, were convinced that its use had greatly decreased the incidence of packing. Alden felt that the pituitrin should be diluted with normal saline so that it can be given slowly.

Bohler and Reiles, agreeing with Stoeckel that tamponade of the uterus increased the mortality at least 100 per cent, reported a series of 200 cases in which they carried out manual exploration of the uterus, following the expression of the placenta, combined with 1 c.c. of pituitrin given intravenously. Their morbidity was slightly over 10 per cent with no mortalities.

The most recent and careful investigation was carried out by two Italians, Debiasi and Romussi, and reported in January, 1935. Using the Frey hysteogram, they found that the marked tetanic contractions occurred immediately after the injection and lasted from two to seven minutes. During the next seven to fifteen minutes, slight variations in contraction and relaxation were noted, but following this period the contractions became regular as in the normal cases. In their series of 54 cases they had 6 failures and 3 poor results, but they were able to explain these satisfactorily on the basis of other findings. They felt that intravenous pituitrin had no value in cases of placenta previa, since the bleeding was from the lower uterine segment which is not contractile. Because of the feeling of Poiche, Claude, Porak and Roulieu that pituitrin disturbs the conductive system of the heart and may cause complete dissociation, these investigators followed four of their cases with electrocardiograms, but could not substantiate such an observation, although they recommended that only 0.5 c.c. be used in cases with myocardial disease. Only one possible mild reaction was noted in all these cases.

More recently Baron has given 1 minim of pituitrin intravenously for induction of labor. He apparently obtained good results, although marked tetanic contractions with the loss of the fetal heart for periods as long as six minutes were often observed.

The present study consists of 96 cases of postpartum hemorrhage in which intravenous pituitrin was employed. It covers the period from September, 1934, to October, 1935, and does not include cases of cesarean section, although pituitrin intravenously is used routinely in these cases. The blood loss was measured by the method recently described by the author. For years we have arbitrarily taken 600 c.c. as the dividing line between normal and abnormal bleeding. However, because it has been shown by the author and other observers that the blood loss increases with the weight of the patient, and that conversely, the seriousness of the hemorrhage decreases with the weight of the patient, it would be better, from a prognostic and comparative standpoint, to express the blood loss in terms of the body weight. At the present time a detailed study is being conducted along these lines and the results will be presented in the near future.

Since the opening of the Woman's Clinic in September, 1932, pituitrin has been used intravenously in varying dosage. During this period, the dosage has been gradually reduced from 0.5 c.c. to 1.5 minims of surgical pituitrin (Units 20) diluted in 2.5 c.c. of normal saline. We feel that the smaller doses have the same therapeutic effect with a somewhat lower incidence of pituitrin reaction and that

the dilution makes it possible to give the medication slowly. For convenience and readiness we have found it advisable to have this dilution ready in the delivery rooms at all times. It is prepared daily by adding 1 c.c. of pituitrin to 24 c.c. of normal saline in a sterile flask sealed with a vaccine stopper. The required amount can be withdrawn quickly and with safety. We have not noted any deteriorating effect or increase in the incidence of pituitrin reaction.

In Table I the 96 cases are analyzed as to the cause of bleeding and the results obtained. Obviously the best results were obtained in the

TABLE I

DIAGNOSIS	CASES	GOOD CONTRACTION	CONTROL OF BLEEDING	REACTION
Atony	22	22	20	1
Partial separation of the placenta	14	14	14	1
Perineal and vaginal lacerations	12	12	5	0
Prolapse of uterus	14	13	2	1
Mismanagement, hemorrhage with placenta	13	11	4	0
Cervical lacerations	5	5	0	1
Myomata uteri	4	3	2	1
Placenta previa, marginal low implantation	4	4	3	0
Premature separation of the placenta	3	3	3	0
Retained placental tissue or membranes	3	3	0	0
Partial inversion of the uterus	2	1	1	0
Total	96	91	54	5

cases of true atony. There were two failures in this group, in one of which there was a question of prolapse of the fundus, since the bleeding stopped during packing when the uterus was brought up into the abdomen; and in the other, the patient had had a former cesarean section and the bleeding was possibly from the site of the previous uterine incision, since the fundus was well contracted. In the group in which the bleeding was due to partial separation of the placenta, the results were excellent but not necessarily due to the action of pituitrin. In these cases the bleeding occurred before the expression of the placenta, and following its removal, either manually, as was done in six cases, or spontaneously, the bleeding stopped, and the pituitrin was given more or less routinely because of the extent of the hemorrhage. The same is true in the cases of mild premature separation, although there was no evidence of excessive bleeding or atony. Only one case of marginal placenta previa is included, since the more severe types are usually treated by cesarean section. The other three cases are of low implantation of the placenta, according to the clinical history and the findings in the placentas. In all of these cases pituitrin intravenously had good results.

In the other cases, the intravenous pituitrin was helpful only so far as it controlled the bleeding due to atony associated with the main cause of bleeding. There was only 50 per cent success in the cases of myomata uteri. In one of these, packing was resorted to, and in another there was a secondary hemorrhage which required transfusions but no packing. The location of the myomas is probably responsible for this variation. One of the cases of partial inversion was a private patient and the condition was noticed several minutes after the patient had received pituitrin intravenously. This was corrected by packing. The other case of partial inversion occurred ten minutes after the expression of the placenta while clots were being expressed. This patient received pituitrin intravenously at that time and the inversion corrected itself without packing.

Notwithstanding the investigation of Debiasi and Romussi, one should realize the possibility of relaxation after the strong tetanic contraction, and ergot or other oxytocics should be given. In one of our cases pituitrin alone was used intravenously, and five hours after delivery there was a secondary hemorrhage of 500 c.c. and evidence of mild shock. Such bleeding could have been prevented by the administration of other stimulants in addition to the pituitrin intravenously.

In five of our cases there was a pituitrin reaction, as manifested by cyanosis, disturbance of the pulse rate, and appearance of shock. In one case a bradycardia of 40 was noted, while in the others a tachycardia was the prominent feature. While most of these reactions were mild and temporary, serious consequences may result, as was shown in one of the cases. This patient died a short time after delivery, and since the cause of death has not been definitely determined, it is conceivable that it was due to pituitrin given intravenously. A résumé of the clinical history is as follows:

The patient was thirty-nine years of age and had had two miscarriages but no full-term pregnancies. She presented herself to the gynecologic clinic with the history of amenorrhea of four months' duration. The diagnosis of pregnancy complicated by myomata uteri was made, and because of a systolic murmur over the apex, she was subsequently examined by the cardiac consultant who ruled out the possibility of cardiac disease. She was followed in the dystocia clinic for several months and during that time the myomatous nodule, which was about 9 cm. in diameter and completely filling the culdesac during the early months of pregnancy, had risen into the abdomen. The pelvis was measured as normal. The patient was admitted to the hospital in mild labor on Jan. 28, 1935. At that time there was no evidence of disproportion, the fetal head being just above the spines. After a labor of twenty-six hours, with a second stage of fifteen minutes, the patient was delivered by midforceps because of fetal distress, the fetal heartbeat being 80 per minute. Up to this time the patient's condition had remained good, the pulse and respirations being normal. There was no evidence of cardiac failure. The placenta was expressed five minutes later without difficulty. Following this, there was some bleeding from the episiotomy but none from the uterus. Because of the diagnosis of myomata uteri, 1.5 minims of pituitrin were given intravenously. Two minutes later, the blood loss being 400 c.c., the patient began to show evidence

of shock. The pulse was of poor quality and ranged around 160. There was cyanosis of the face and the blood pressure could not be obtained. Intravenous glucose (10 per cent) was given and her condition improved, the systolic pressure being 90. Believing that this reaction was due to shock, and since there was still slight bleeding from the episiotomy, 1 c.c. of pituitrin was given intramuscularly thirty-three minutes after the intravenous injection. Five minutes later the patient's condition suddenly became worse. The respirations became shallow, the blood pressure could not be obtained, and frothy bloody sputum appeared at the mouth. In spite of caffeine, adrenalin, and atropine the respirations ceased ten minutes later. The impression at the time was cardiac failure with pulmonary edema. The total blood loss was measured as 700 c.c. An autopsy was not obtained.

The significant facts in this case are: (1) The intravenous pituitrin was given prophylactically, since there was no atony or uterine bleeding, and (2) evidence of shock appeared after each of the injections. Although this is not a clear-cut case of death due to pituitrin reaction, it should impress upon us the fact that any medication which produces a generalized reaction, however mild and temporary it may be, might in some cases produce serious and lasting effects.

The cause of these reactions is not yet clear. In this series, most of the patients had received pituitrin intramuscularly prior to the intravenous injection, and this may account for the high incidence of reactions. Moreover, in our own experience, pituitrin reactions are seldom noticed in cases of cesarean sections where general anesthesia is used. These observations support the theory of Alden that pituitrin reactions are manifestations of sensitivity to the drug. For that reason we are employing, at the present time, an equivalent amount of pitocin which is protein-free.

Table I shows that pituitrin was given intravenously in practically all types of bleeding. It was of no therapeutic value in 42 of the 96 cases. This is due to the prevailing impression that most of the postpartum hemorrhages are due to atony of the uterus. In fact only 23 per cent of the hemorrhages in this series, and 9 per cent in a series previously studied, were due to this cause. Every physician should be familiar with all the causes of bleeding in each of the three phases of the third stage. Partial separation of the placenta, cervical lacerations, and episiotomies or perineal lacerations are the most frequent causes of bleeding before the expression of the placenta. Excessive bleeding with the expression of the placenta is due to faulty management of the third stage of labor. Following the expression, atony, prolapse of the fundus, and cervical and perineal lacerations are the most frequent factors in the production of excessive blood loss. With such knowledge, the suitable therapy can be instituted immediately. If atony is present, and this can be determined quickly, it is useless to attempt to control the bleeding with intramuscular injections of pituitrin or ergot since they require four to five minutes to act. Intravenous therapy should be instituted at once. Of course, permanent

advancement along this line will be made only when we discover the causes of atony and thereby eliminate them. More extensive researches in the field of analgesia and anesthesia are necessary.

Another factor which is increasing the blood loss is the tendency to wait ten or fifteen minutes before attempting to express the placenta. Such a practice must be condemned, for the placenta should be expressed as soon as it is separated, regardless of the time elapsing between the delivery and the expression. Such a delay will only lead to the formation of clots behind the placenta and subsequent atony of the uterus. We must appreciate this point, as was so well stated by one of our internes in explaining a hemorrhage due to this cause: "At the time it did not seem rational that the placenta had separated immediately following the delivery of the child."

CONCLUSIONS

1. From the literature and our own experience, intravenous pituitrin in the third stage of labor is reliable, quick, and intense in its action. It is specific for atony of the uterus only.

2. One and a half minims of surgical pituitrin (Units 20), diluted in 2.5 c.c. of normal saline, are used in this clinic. This dilution makes it possible to give the medication slowly.

3. Reactions were noted in 5 of the 96 cases. In one of them it may have been responsible for the death of the patient.

4. Intravenous pituitrin should not be used indiscriminately, but only in the cases of atony of the uterus. In these cases it should be given as soon as the diagnosis is made. Intramuscular injections of pituitrin or other oxytocics are useless in the control of atony because they require four to five minutes to produce the desired effect.

5. Atony of the uterus is not the only cause of postpartum hemorrhage. It was responsible for only 23 per cent of the hemorrhages in this series. A knowledge of the management of the third stage and of the other causes of excessive blood loss is indispensable.

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FETAL HEART DILATATION; PULMONARY CONGESTION
AND PULMONARY EDEMA NEONATORUM;
"CONGENITAL PNEUMONIA"; ASPHYXIA*

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UP TO quite recently, asphyxia was considered the main cause of death of the fetus in utero and of the stillborn. The seat of the trouble was believed to be primarily in the respiratory system. All efforts were therefore concentrated on getting air into the child's lungs, and drastic methods were used which were frequently injurious. Very little consideration was given to the underlying causes that interfered with the proper functioning of the respiratory apparatus.

With the performance of more frequent autopsies, it has become evident that asphyxia is not the primary or underlying cause of death of the fetus in most cases, but that asphyxia is secondary to other conditions. Injuries to the fetus, in which cerebral hemorrhage is the main lesion, were found to be the most frequent cause of asphyxia and the death of the fetus. But there still remain a great number of unexplained or wrongly interpreted cases of fetal and neonatal deaths.

When the fetus dies before birth from compression of the cord, the separation of the placenta or from any other cause, it is believed that, due to the increase of CO_2 , the fetus first makes an effort to breathe, and as respiration is impossible, it is asphyxiated. But that is not necessarily the way death occurs, for the accompanying decrease in oxygen, anoxemia, depresses the vital centers, and the fetus dies, in most cases, without the respiratory center being stimulated to action and without the fetus making any attempts at respiration. These deaths, therefore, cannot be designated as due to asphyxia.

Atelectasis as a cause of neonatal death is, I believe, grossly exaggerated. Infants, the same as adults, can live with a considerable portion of their lungs collapsed. Atelectasis as a primary condition occurs rather infrequently.

Johnson and Meyer state: "It should be recognized that in all cases atelectasis is secondary to some primary cause." The real cause of death is the primary condition. When on autopsy a baby shows atelectasis, we should determine further what lesion prevented the lungs from expanding. The term atelectasis as a cause of death is used mostly to cover up unknown causes.

The respiratory apparatus does not function during intrauterine life. It is fully developed at about seven months, but lies dormant until the time comes for it to be set in motion by the proper stimulus. When the baby is born, the placenta separates immediately, and the consequent

*Read at a meeting of the Section of Obstetrics and Gynecology of the New York Academy of Medicine, December 17, 1935.

increase of CO_2 in the placental-fetal circulation together with the external skin irritation stimulate the respiratory apparatus so that the baby breathes. When respiration is delayed or when the infant fails to breathe, the assumption is that the respiratory apparatus is at fault and the condition is designated as asphyxia. But as the respiratory apparatus does not function intrauterine, it is not subjected to any strain and is, therefore, not likely to be out of order. When it fails to react, it is due to a lesion in some vital structure or to a failure of the proper stimulus to reach the respiratory center. As the stimulus to the respiratory center comes through the circulation, it is to the circulatory system that we must give our attention and determine the factors that disturb it.

In a previous paper entitled, "The Slowing of the Fetal Heart and Its Relation to the Fetal-Placental Circulation," I indicated that the slowing of the fetal heart is not due to an increase of CO_2 , which is supposed to stimulate the vagus, but that it is produced directly by the contraction of the uterus, compressing the placenta and forcing a variable amount of blood out of the placenta into the fetus. This increases the volume of blood in the fetus and raises the arterial and venous tension in the fetal circulation. This increased tension produces the slowing of the fetal heart (Figs. 1 and 2). The increased volume of blood and increased tension produce a syndrome, of which the slowing of the fetal heart is one of the early manifestations. The syndrome includes, in addition to the slowing of the fetal heart, the passing of meconium, the stopping of the heart, hemorrhages in the fetal organs, death of the fetus at the onset of labor, and other manifestations.

The increased tension in the fetal-placental circulation also produces congestion and hemorrhage in the placenta itself. This accounts for the lesions recently described by Goodall, which he found in two-thirds of the placentas examined.

The overloading of the circulation also directly overloads the fetal heart. The auricles and ventricles are overfilled with blood, the heart becomes distended and dilated, it is prevented from contracting, and therefore ceases to function. Consequently a condition of acute cardiac dilatation occurs in the fetus.

When the overloading of the circulation occurs with the last one or two labor pains, and the baby is delivered, the baby's heart will still be overloaded and dilated. When the infant starts breathing and the lungs expand, there is a stasis in the pulmonary circulation due to the dilated heart, and as a result of it, pulmonary congestion occurs. This is made evident by crepitant râles which can be heard over the chest. The râles will vary in extent depending upon the degree of congestion.

When the overloading of the heart is more severe, particularly in those cases where the fetal heart rate had dropped so low that it had been necessary to deliver the baby quickly, the dilatation of the heart is

greater, the pulmonary stasis is more severe, so that besides the congestion there occurs a pulmonary edema. This is evidenced by bubbling râles over the entire chest, with considerable quantities of serum in the mouth and throat.

These physical signs were ascertained by listening to the chest with a (sterile) stethoscope as soon as the babies were born. When the baby is delivered it is held up by its legs for a few seconds, until it takes

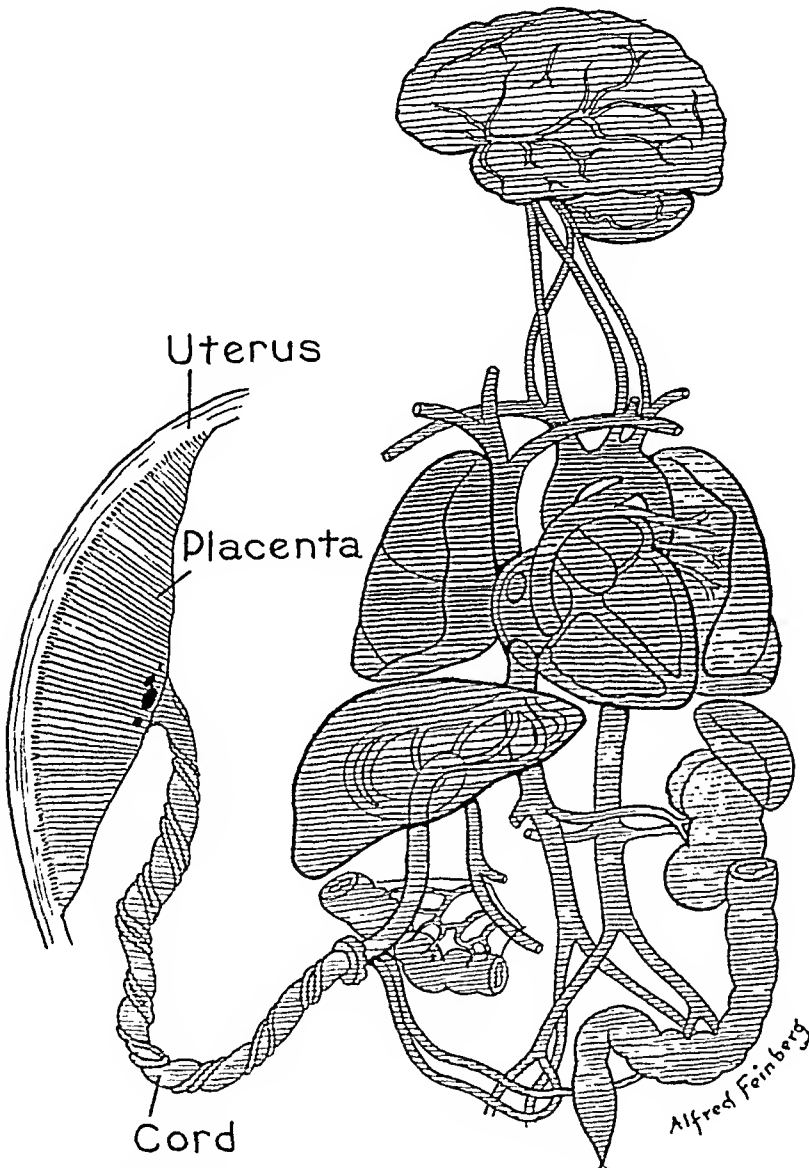


Fig. 1.—The fetal-placental circulation in the interval between a labor pain. The light shading represents the circulation in the blood vessels and organs under normal tension.

one or two good breaths, and to permit the contents of the mouth and throat to drain out. It is then laid down and the chest is auscultated. In the great majority of cases the normal breath sounds with the normal heart sounds can be heard, but where there has occurred some embarrassment of the circulation, as evidenced by the slowing of the

fetal heart, we get the signs of pulmonary congestion, and less frequently the signs of pulmonary edema.

As the heart regains its tone, the congestion and edema clear up and the sounds become normal. I have not as yet used any medication for this condition. It might be advisable to treat the condition as we usually do cases of cardiac dilatation with pulmonary edema.

With the pulmonary congestion and pulmonary edema, there may also take place, due to the increased tension in the circulation, rupture of the

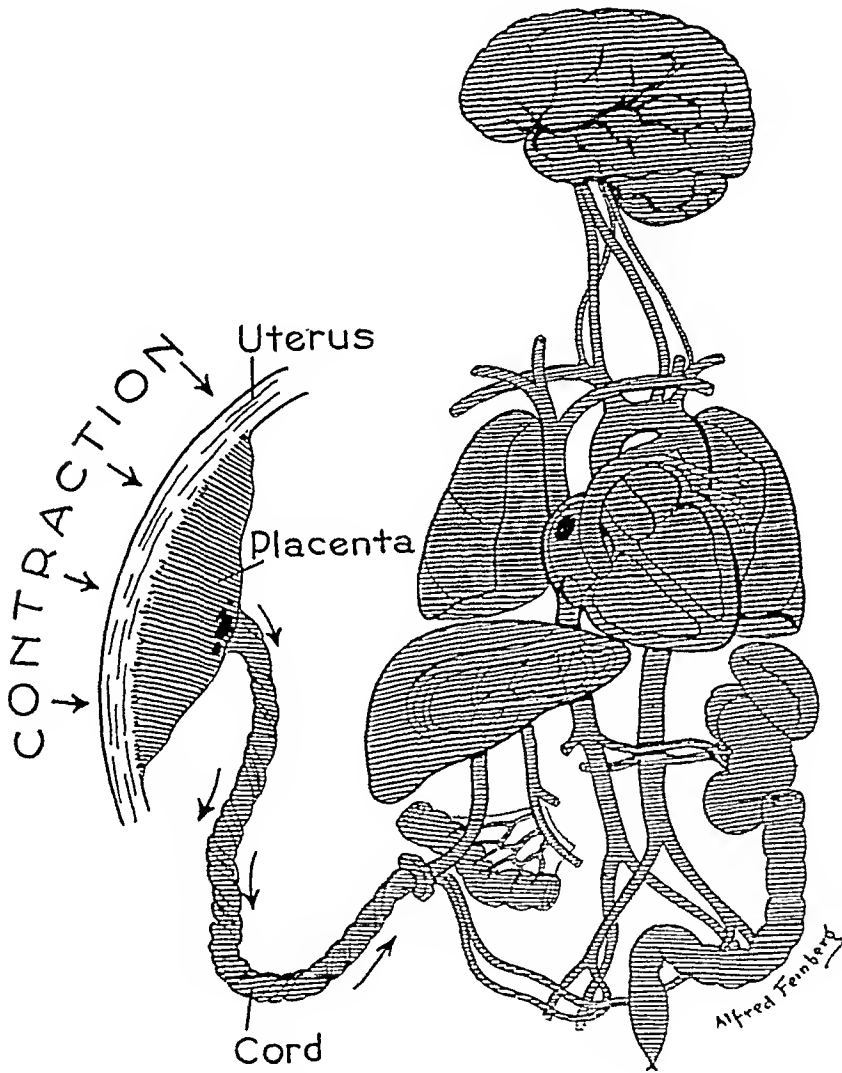


Fig. 2.—The fetal-placental circulation during a strong uterine contraction. The placenta is compressed and blood is forced out of the placenta into the fetus. The dark shading represents the increased tension in the circulation, with the blood vessels distended, the heart dilated, and the organs congested.

blood vessels in the lungs with the bringing up of fresh blood. The condition then becomes much more serious.

We should give some consideration to the possible damage that the heart may sustain from such intrauterine cardiac dilatation. If the baby survives we must consider whether the heart recuperates entirely or whether it remains permanently weakened. It is possible that the

shortness of breath of some children and their inability to exert themselves, which may be associated with poor heart tones, are the result of this cardiac strain at the very beginning of life. This condition of the heart warrants further study.

As the baby is held up by its legs with the head down, all the contents of the bronchi, trachea, throat, and mouth should run out. But frequently serum and mucus accumulate in the throat again. It has been rather puzzling how to account for the source of this mucus. It has always been assumed when the infant's chest is "full of mucus" that it had swallowed or rather aspirated the mucus in its passage through the birth canal. But that is not so, as in head presentations we know that the baby does not breathe until the head has left the vagina. It had to be presumed that it swallowed this mucus when no other explanation was forthcoming. It is my belief that the "mucus" in the chest is not aspirated, but that it is the amniotic fluid normally present in the respiratory tract, and the serum of pulmonary congestion or pulmonary edema caused by the dilatation of the fetal heart. When the infant's mouth and throat continue to fill up with serum, crepitant or bubbling râles can be heard in the chest; and conversely as long as these râles are present the infant continues bringing up serum from the lungs.

In considering the trachea and bronchi in the fetus, one gets the impression from textbooks and the literature that in the fetus they are empty and do not contain anything. A consideration of the anatomy of these structures will show that this is not possible. The trachea and bronchi have cartilaginous rings in their walls which hold them open and prevent them from collapsing. Any cavity whose walls cannot be approximated must hold something, it cannot remain a vacuum. In the world at large all so-called empty spaces are filled with air, but as there is no air intrauterine when the membranes are intact, the trachea, bronchi, and bronchioles must be filled with whatever substance that surrounds them. Therefore, these cavities in the fetus must be filled with amniotic fluid. As respiration does not take place intrauterine, there is nothing unphysiologic or objectionable in having amniotic fluid occupying these spaces. The amniotic fluid fills all the open cavities in the fetus, such as the external ear, the nose, mouth, throat, trachea, and bronchi. The amniotic fluid does not normally enter the lungs, as the lungs are collapsed, although it is possible that amniotic fluid does penetrate some of the proximal alveoli.

When the membranes rupture and the amniotic fluid escapes, air enters the uterine cavity. The amniotic fluid then can run out of the bronchi, the trachea, and mouth, and can be replaced by air. This occurs in head presentations, but in breech presentations, as the head is at a higher level than the trachea, the amniotic fluid cannot drain out, not until at the time of delivery, when the body is raised above the level of the head.

A number of observers have described a condition which they have found at autopsy in the lungs of stillborn infants, and in those that have died soon after birth, as congenital pneumonia. Some of the later papers on the subject are by Johnson and Meyer, Farber and Smith, Kalder, and Warwick.

It is believed that this form of pneumonia starts during intrauterine life and is produced either by bacteria or amniotic fluid or both. But all the observers of this condition find difficulty in explaining how bacteria could get into the fetus to cause the pneumonia. Also, to account for the fact that bacteria were found in only a small percentage of the cases, and only in those babies that lived for some time or in which the autopsy was not done promptly. The theory that amniotic fluid by chemical irritation may be the cause of these pneumonias is assumed because the bacterial cause fails to satisfactorily account for the condition. Clinically, the infants do not have any fever and do not show physical signs or symptoms of pneumonia. Pathologically, on gross examination the lungs do not suggest pneumonia, there is no pleuritis, the lesions are always bilateral, and resemble hemorrhage, and atelectasis with congestion. The diagnosis of pneumonia is made entirely on the microscopic findings.

It is my belief that this pathologic condition is not pneumonia in most of the cases so considered. The condition is a pulmonary congestion, pulmonary edema, and pulmonary hemorrhage, produced by the overloading of the fetal circulation in the manner already explained above. This condition may be associated with fetal heart dilatation, or with hemorrhage in the brain or other organs. The amniotic fluid that is found at autopsy in these "congenital pneumonias" comes from the trachea and bronchi which, as indicated above, normally occupies these cavities. As the condition is not pneumonia, there is, therefore, no need of trying to explain its exciting cause by bacteria or by amniotic fluid irritation.

It occasionally happens that a baby delivered by cesarean section and not subjected to unsuccessful attempts at delivery or to a prolonged labor is, for no apparent reason, stillborn. The death of the baby may be due to the practice of some operators of ordering the intramuscular injection of an ergot preparation, while they are scrubbing up, or the injection of pituitrin at the start of the operation, in order to have the uterus contract sooner and lessen the bleeding. But apparently little consideration is given to the effect these injections can have on the fetus in the meantime. The ergot or pituitrin in some cases causes a tetanic contraction of the uterus, which compresses the placenta and forces blood out of the placenta into the fetus, thereby overloading the fetal circulation, and stopping the fetal heart or causing hemorrhages in the vital organs and death of the fetus.

The authors of the papers on "congenital pneumonia" mention cases which were delivered by cesarean section and were stillborn, and on autopsy they found lesions in the lungs which they assumed to be pneumonia. This was accompanied in some cases by hemorrhages in other organs. They are at a loss to explain how the pneumonia occurred. As indicated above, these lesions are not pneumonia but congestion and hemorrhage, and death was caused by the overloading of the fetal circulation.

Another cause of fetal death during cesarean section is due to the excess loss of blood from the fetus. In incising the uterus, the placenta is often cut through and blood escapes from the placenta and consequently from the fetus. While a variable amount of blood can escape from the placenta without any serious effect on the fetus, we cannot judge the amount that the fetus is losing or how much loss it can stand without serious consequences. A fatal exsanguination may occur in a very short time. If the incision in the placenta happens to be near the insertion of the cord, the bleeding will come directly from the fetus and the fetus will succumb sooner. It is, therefore, advisable, when the placenta is cut into, to search for the cord and clamp it immediately before delivering the baby.

As a rule, respiration is delayed longer in cesarean babies than in those delivered from below. The reason for this is, I believe, because of the loss of blood from the incised placenta, an anemia is produced in the fetus, which delays the stimulation of the respiratory center. Also after forceps delivery the baby does not breathe as promptly as it does in spontaneous deliveries. In a spontaneous delivery, the contraction of the uterus forces the baby out, and at the same time forces blood from the placenta into the fetus; the respiratory center, therefore, receives an abundant supply of blood and is promptly stimulated. In forceps delivery and in cesarean section, the uterus is not sufficiently contracted while the baby is being extracted, so that the placenta is not compressed and the baby thereby gets less blood in its system and this delays the stimulation of the respiratory center.

As the circulatory system plays such an important rôle in the welfare of the fetus, the necessity of constantly watching the fetal heart is evident. During the second stage of labor, it is not sufficient to listen to the fetal heart occasionally, but it is necessary to watch the fetal heart rate constantly. Toward the end of the second stage it is absolutely essential that the fetal heart be auscultated after each and every pain. Babies are frequently lost with the last one or two labor pains. When the head is on the perineum and the uterine contractions are strong, the fetal circulation is then under the greatest tension and the fetal heart may be dangerously embarrassed. Babies are thereby lost in the last few minutes of delivery. Holding the head back for any length of time to protect the perineum is not good practice, as it does not save the

perineum and endangers the child. An episiotomy done at this stage is of greater advantage to the perineum and a relief to the baby.

With the writer's heavy-weighted stethoscope the nurse can easily auscultate the fetal heart while the woman is on the delivery table, without disturbing the sterile drapes. When the fetal heartbeat remains normal until the end of the delivery, the baby is bound to be in good condition when it is delivered and will not need resuscitation. The most important part in the treatment of asphyxia neonatorum is its prevention; and that can be accomplished by watching the fetal heart constantly, and avoiding injury to the baby during delivery.

When the baby is born, it should be held up by its legs with its head down. This is the best means of having the amniotic fluid drain out of the baby's mouth, throat, trachea, and bronchi. This allows gravity to clear out all the passages. Suction with a catheter cannot clear out the trachea or bronchi as effectively as gravity. While the child is in the inverted position, the lower jaw is compressed against the upper jaw, and with outward pressure from the neck to the chin the contents of the mouth are expelled.

When the baby is held in the inverted position, more blood goes to the medulla and stimulates the respiratory center sooner. I find that babies breathe sooner if they are held in the inverted position than when they are laid down as soon as delivered.

As stated above, when the fetal heart rate has been good and the baby is not injured, the baby should breathe in a few seconds after it is born. When it fails to breathe, the child should receive immediate attention. All violent methods, rough handling, and cold plunges are condemned. But we cannot leave the baby alone entirely with the hope that it will start breathing. At birth the baby is in a state of apnea, with the accumulation of CO_2 , the hypercapnia stimulates the respiratory center. But while CO_2 is accumulating and the baby does not breathe, there occurs at the same time a diminution of oxygen, producing a state of anoxemia. This anoxemia can in the meantime depress the medulla to such an extent that the CO_2 will fail to stimulate it to action. For that reason it is not advisable to wait any length of time before getting the baby to breathe. Delayed respiration or improper heart action causing a stasis in the circulation at birth may so interfere with the proper oxygenation of the vital centers and the brain as a whole, that they may become damaged in a very short time. Anoxemia is a dangerous condition, especially for the immature brain cells of the newborn. As Haldane says, "Anoxemia not only stops the machine but wrecks the machinery." It is possible that the child may suffer permanent damage as a result of the temporary anoxemia. The retarded mentality of some children, coming from intelligent parents, may be due, aside from other causes, to damage to the brain sustained at the time of birth from anoxemia.

In order to avoid delay in respiration, if the baby fails to breathe spontaneously and promptly, mouth to mouth respiration should be used. I prefer this method to any other, as it is immediately available and is most effective. The baby should be kept warm during the procedure. I consider the time element an important factor. With this method a heart that is hardly perceptible or very slow commences to beat forcibly and more rapidly. While if we wait for other means of resuscitation, the heart may stop entirely in the meantime.

SUMMARY

1. Asphyxia as a cause of fetal and neonatal death is usually secondary to some other lesion; as a primary cause it occurs rather infrequently.

2. Death of the fetus intrauterine is not produced through asphyxia but directly from anoxemia.

3. Atelectasis as a primary cause of death occurs rarely, it is mostly secondary to, and associated with, other lesions.

4. It is the circulatory system that is most frequently involved in the death of the fetus.

5. The contraction of the uterus compresses the placenta and forces blood out of the placenta into the fetus and overloads the fetal circulation. This produces a syndrome, which includes the slowing of the fetal heart, the passing of meconium, the stopping of the fetal heart, hemorrhages in the fetal organs, death of the fetus at the onset of labor; and fetal heart dilatation, which in turn causes pulmonary congestion and pulmonary edema neonatorum.

6. When the baby's chest is "full of mucus" it is due to pulmonary congestion and pulmonary edema, and only occasionally to aspiration.

7. The trachea and bronchi of the fetus are not empty, but are filled with amniotic fluid.

8. "Congenital pneumonia" cannot be considered as an entity, the pathologic findings are due to pulmonary congestion, pulmonary edema, and pulmonary hemorrhages.

9. In cesarean section, death of the fetus may be due to the overloading of the fetal circulation from the use of pituitrin or ergot. Also from the excess loss of blood from the incised placenta.

10. Delayed respiration at birth produces anoxemia which may cause damage to the brain.

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AN OPERATION TO CORRECT GENITAL PROLAPSE FOLLOWING VAGINAL PANHYSTERECTOMY*

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THERE is still considerable difference of opinion as to which is the best operative procedure in the treatment of complete uterine prolapse. Some routinely employ the Mayo operation, which has as one of its important steps the vaginal removal of the entire uterus. One advantage of this operation is that the possibility that the patient may develop a uterine carcinoma in later life is entirely eliminated. On the other hand, another group of gynecologists prefer the Watkin's interposition operation, or vaginal fixation as it is sometimes called, for cases of prolapsus uteri and reserve the vaginal panhysterectomy for those patients who have in addition to the prolapse other pathologic conditions in the uterus, such as small fibroids.

An interposition operation is easier to perform and less shocking than a vaginal panhysterectomy, but the main reason for my own preference for the former operation is that it has yielded such excellent results. In 1926 I reported a series of 60 patients with uterine prolapse operated upon by Cullen and myself and studied postoperatively. One woman had a return of the cystocele after being well for ten years. In the other 59, all of whom were traced, the interposition operation apparently permanently cured the prolapse. Everett² reported a postoperative study of the cases operated upon at the Johns Hopkins Hospital for uterine procidentia and compared the results obtained by the interposition operation with those following vaginal panhysterectomy. He concluded that the Watkin's interposition operation is the procedure of choice for the treatment of prolapse of the uterus in women past the menopause.

The interposition operation certainly has this one most important advantage over a vaginal panhysterectomy, namely, that when failure occurs a much more serious condition develops when the uterus has been removed. When an interposition fails, there is usually merely a return of the cystocele or rectocele and a simple plastic operation will correct the condition; and even if the uterus comes down, one can still try the interposition operation again, suturing the fundus of the uterus to the periosteum of the symphysis as recommended by George Gray Ward.

On the other hand, when a genital prolapse develops after a panhysterectomy, a condition results which is more difficult to correct.

*Read before the Baltimore Obstetrical and Gynecological Society on February 15, 1936.

In fact some gynecologists feel that no satisfactory operative technic has yet been worked out for curing such a prolapse. The anterior and posterior vaginal walls roll out and become lengthened, and before long a true hernia of the pelvis develops. Probably a colpectomy has been the operation most frequently performed for genital prolapse after a panhysterectomy, but it is difficult to carry out properly and if successful the sexual life of the woman comes to an end.



Fig. 1.—Shows the genital prolapse. The scar from the previous operation (a vaginal panhysterectomy) can be plainly seen.

One year ago I had the opportunity of operating upon a patient with a marked genital prolapse following vaginal panhysterectomy. The condition was entirely corrected by the operation. The woman now has no urinary symptoms and the bladder has a capacity of 500 c.c. Moreover she has been left with a vagina of normal length and diameter so that sexual relations are possible. The operation performed on this patient, while not demonstrating any entirely new principles, does bring out certain modifications in technic which, I believe, have not been previously reported.

A. M., aged fifty-eight, was admitted to St. Joseph's Hospital, Baltimore, May 3, 1935, complaining of vaginal prolapse. The family and general history were unimportant. The menstrual periods stopped at the age of fifty. The patient had had three children. She had noticed for ten years that "her womb came down." She had been operated upon in December, 1933, for uterine prolapse at one of the Baltimore hospitals. While in the hospital, she was found to have diabetes mellitus for which insulin was prescribed. Within a few months after the operation the patient again noticed that "something came down." She tried using a ring pessary but this gave no relief. She decided to submit to another operation and was admitted to my service at St. Joseph's Hospital. The general physical examination was essentially normal. The urine showed a small amount of sugar which promptly disappeared when the patient's daily dose of insulin was slightly increased. Pelvic examination showed that there was a marked genital prolapse. When the patient strained or stood up, the apex of the prolapse descended 10 cm. below the vaginal orifice. There was fortunately no ulceration of the prolapsed tissues. The patient was kept in bed several days prior to operation, and daily vaginal douches were given.

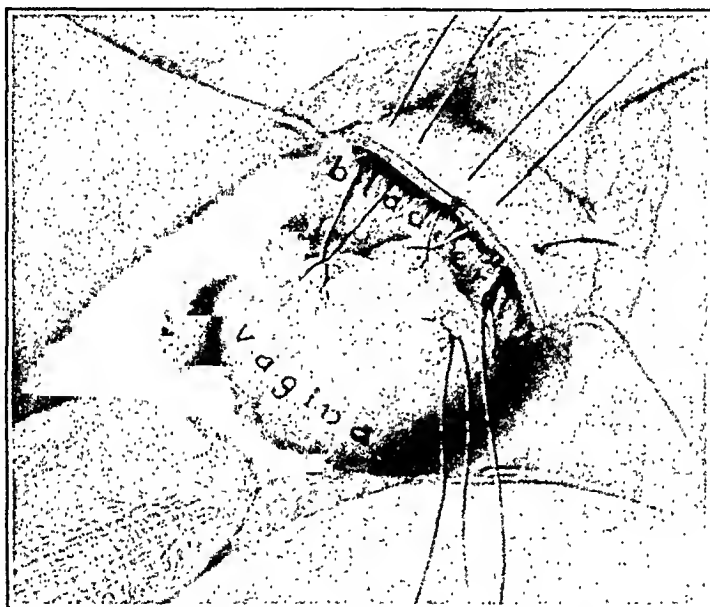


Fig. 2.—The vagina is being sutured to the lower part of the abdominal fascia. This pushes the bladder forward. The recti muscles are shoved laterally as the stitches are introduced through the peritoneum and fascia. It is to be noted that the fascia in the lower part of the wound has not been divided, although the skin incision goes all the way down to the symphysis pubis. One of the elongated round ligaments can be seen on the left side of the picture.

Operation: May 14, 1935. The vagina was first carefully scrubbed with soap, alcohol, and ether, and then painted with Scott's solution. A midline incision through the skin and fat was then made from a little below the umbilicus down to the symphysis pubis. The fascia and peritoneum were divided in the upper half of this incision but not in the lower half. An assistant with his finger in the vagina then pushed the prolapse upward until the vagina could be clearly identified by the operator. A Cameron light introduced from below into the upper part of the vagina facilitated the identification of structures. The bladder itself had hypertrophied as a result of being prolapsed for so many years. Three medium-sized braided silk sutures were then introduced from above into the top of the vaginal vault which had been pushed upward by an assistant. These sutures were made to pass through the peritoneum, to pass on either side medially to the recti muscles which were pushed laterally, and finally to pass through and come out above the fascia of the recti muscles. The two ends of each of these sutures were then tied together above

the fascia of the recti muscles. This step in the operation fixed the vagina to the anterior abdominal wall with three mattress sutures. One of these sutures passed directly through the midline and the other two were close to it. All were medial to the inner borders of the recti muscles. When the operation was completed, the knots lay above the fascia but below the skin and subcutaneous tissue. Two points in technic should be emphasized. First, that these sutures do not go through the skin and, second, that they must be of nonabsorbable material. They are per-

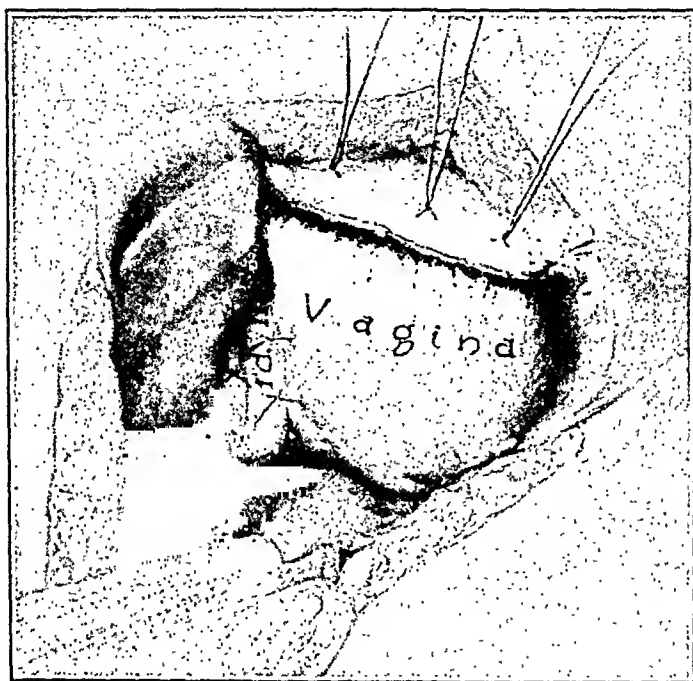


Fig. 3.—The vagina has now been sewed to the peritoneum and rectus fascia. In order to prevent the bladder from bulging laterally around the vagina which does not reach all the way across the pelvis, the elongated round ligaments are plicated and sutured to the vagina. The drawing shows this step in the operation completed on the left side.

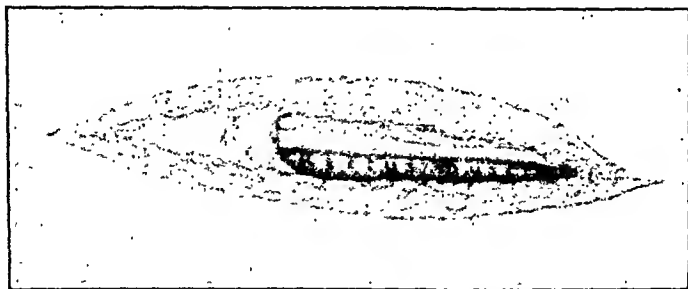


Fig. 4.—Shows the position of the fixation sutures after they have been tied and indicates the approximate length of the skin and fascial incisions. One of the fixation sutures lies directly in the midline and the other two are close to the midline. They have all been brought through the peritoneum and fascia medial to the rectus muscles.

manent sutures and not to be removed after a few weeks. In these and several other features this operation differs from the one described by Fraenkel, in 1920, and recommended by Jarcho in an article published in 1928.

In the former operation upon this patient the surgeon had followed the usual procedure of sewing the round ligaments back to the vaginal vault after he had removed the uterus. As the genital prolapse developed after the hysterectomy, the

round ligaments were stretched and became lengthened. Now in the second operation, as the vaginal vault was drawn up, the round ligaments were also drawn upward. On either side of the vagina, which was now fixed to the anterior abdominal wall, the round ligaments appeared V-shaped. One leg of the V started at the place at which the round ligament entered the peritoneal cavity from the inguinal canal, and then dipped down into the pelvis for some distance. The round ligament finally turned upward again ending as the top of the other leg of the V at the point where the vagina was now attached to the abdominal wall. Of course, I do not know whether or not the round ligaments would always lengthen in cases of genital prolapse in the way that they did in this case, but certainly this V-shaped formation exhibited by both round ligaments was of definite help in operating upon this patient. For while it was evident that the fixation of the vagina to the anterior abdominal wall would correct the vaginal prolapse, it appeared as if the hypertrophied bladder which now could not prolapse in the midline because of the diaphragm which the vagina now formed in the midline, could still bulge laterally around this diaphragm, but by employing the additional procedure of sewing the two limbs of the V-shaped round ligaments together on either side and to the vagina, these lateral openings were closed, thus helping to hold the bladder forward and preventing it from getting around the vagina. After completing the abdominal operation a perineorrhaphy was performed. There was no necessity for performing an anterior repair, as the abdominal operation had already entirely corrected the cystocele.

The convalescence was uneventful, and she was discharged from the hospital on the twenty-second day after operation. On examination nine months later there was no evidence of any prolapse, either anteriorly or posteriorly, and two fingers could be introduced into the vagina for 10 cm. without causing the patient any discomfort. The bladder has a capacity of 500 c.c. The patient has no urinary symptoms and no other complaints.

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According to the author, patients with toxemias of pregnancy may be successfully treated by the oral administration of alkaline compound tablets, consisting of potassium citrate, sodium bicarbonate, and calcium sodium lactate. Occasionally it is necessary to give a single intravenous dose of calcium alone. Records of 53 patients so treated are given in tabular form, and a series of 131 patients, treated by routine methods in surrounding hospitals, used as controls. It is claimed that acute cases nearly always show an immediate response to treatment by an increased daily output of urine, a fall in the amount of albuminuria, lowering of hypertension, and a disappearance of edema and other symptoms. The use of an ordinary diet is advantageous. Fetal mortality is diminished because induction of labor is not indicated as often in the tested group as in the controls; 2 per cent versus 66 per cent in the control series. The incidence of spontaneous premature labor is lower in the treated group.

WILLIAM F. MENGERT.

THE MICROSCOPIC AND BACTERIOLOGIC STUDY OF URINE OF OBSTETRIC PATIENTS

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FREQUENT difficulties in correlating clinical evidences of urinary tract infection with the urinary findings led to systematic study of the cytologic and bacteriologic characteristics of the urine in a series of pregnant and puerperal women. Results of this study form the basis of this communication.

METHODS

One hundred and fifty women, admitted consecutively in the last month of pregnancy, and an equal number of puerperal patients were observed on the Obstetric Wards of the University Hospitals. Urine specimens were drawn by catheter at any convenient time during the last month of gestation. Postpartum specimens were similarly obtained during the first ten days after delivery, usually on the ninth or tenth day. The glass catheters were sterilized in mercuric chloride solution and were rinsed in running tap water just before use. The urinary meatus was cleansed with small cotton pledgets soaked in 1:2,000 solution of mercuric chloride. The urine for direct microscopic study was collected in clean, nonsterile bottles, that for bacteriologic study in sterile containers.

For direct microscopic examination, the specimen was centrifuged at uniform, low speed for one minute. A drop of the sediment was placed upon a clean slide and covered with a cover glass. Under the high power, dry lens, at least twenty fields were examined, and the average number of pus cells was recorded. The presence of five or more pus cells in one group was taken to indicate clumping, the incidence of which was recorded as +, ++, +++, or +++++. Note was also made of any bodies which resembled bacteria. A similar preparation was allowed to dry on a slide, was then fixed with heat, and stained by Gram's method. This slide was examined with the oil immersion lens for the presence of bacteria.

The specimens collected in sterile containers were studied by one of us (W. W. H.) without knowledge of the clinical or cytologic findings. Clear specimens were centrifuged at moderate speed (2,000 r.p.m.) for fifteen minutes, and the sediments were plated on the surface of blood agar (sheep defibrinated blood). Specimens showing marked turbidity were plated direct with no attempt at concentration by centrifugation. No quantitative determinations were made nor was any special effort directed toward determining the presence of small numbers of organisms. Bacteria producing colonies on the plates were further identified by their staining reactions and cultural characteristics.

RESULTS

Microscopic examination of the centrifuged, fresh urine gave results recorded in Tables I, II, and III.

TABLE I. PUS CELLS IN THE URINARY SEDIMENT (WET MOUNT)

AVERAGE NUMBER OF PUS CELLS PER HIGH POWER MICROSCOPIC FIELD	ANTEPARTUM PATIENTS		POSTPARTUM PATIENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
None	0	0.0	0	0.0
1 to 5	86	57.3	66	44.0
6 to 10	12	8.0	22	14.7
11 to 15	9	6.0	10	6.7
16 to 25	7	4.7	9	6.0
26 to 50	14	9.3	18	12.0
51 to 100	6	4.0	12	8.0
101 to 200	9	6.0	10	6.7
More than 200	7	4.7	3	2.0
	150	100.0	150	100.0

It is remarkable (Table I) that every urine specimen contained some pus cells, and that in 52 (34.6 per cent) of the antepartum and in 62 (41.4 per cent) of the postpartum specimens, there were more than ten pus cells in the average high power field.

TABLE II. "CLUMPED" PUS CELLS IN THE URINARY SEDIMENT

THE EXTENT OF "CLUMPING"	ANTEPARTUM PATIENTS		POSTPARTUM PATIENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
None	114	76.0	100	66.6
+	14	9.3	21	14.0
++	13	8.7	18	12.0
+++	5	3.3	6	4.0
++++	4	2.7	5	3.3
	150	100.0	150	100.0

Considerable "clumping" (more than +) was noted in 22 (14.7 per cent) of the antepartum and in 29 (19.3 per cent) of the postpartum urines. It is evident that many individuals in both groups, who showed a considerable number of pus cells in the urine, did not present the "clumping" phenomenon. On the other hand, it is surprising that such a large percentage presented "clumped" pus cells, a finding which is commonly associated with clinical urinary tract infection.

TABLE III. BACTERIA IN FRESH URINARY SEDIMENT (WET MOUNT)

RELATIVE NUMBER OF VISIBLE BACTERIA	ANTEPARTUM PATIENTS		POSTPARTUM PATIENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
None	20	13.3	14	9.3
+	65	43.3	72	48.0
++	28	18.7	30	20.0
+++	16	10.7	13	8.7
++++	21	14.0	21	14.0

Sixty-five (43.4 per cent) of the antepartum and 64 (42.7 per cent) of the postpartum specimens showed considerable numbers of bacteria on direct examination (wet mount). These figures parallel closely

the number of specimens with more than 10 pus cells per high power field (Table I). Although bacteria were detected usually in direct examination of the urine which showed numerous pus cells, such was not invariably the case.

TABLE IV. BACTERIA IN STAINED (GRAM'S TECHNIC) URINARY SEDIMENT

TYPES OF ORGANISMS	ANTEPARTUM PATIENTS		POSTPARTUM PATIENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
None	39	26.0	9	6.0
Gram-negative bacilli only	52	34.7	60	40.0
Gram-negative bacilli with gram-positive cocci	35	23.3	50	33.3
Other organisms	24	16.0	31	20.7
	150	100.0	150	100.0

It is to be noted that relatively few (26 per cent of antepartum and 6 per cent of postpartum) urine specimens were bacteria-free, as shown by the stained preparations. It was anticipated, from the knowledge of frequent urinary tract invasion by the colon bacillus, that gram-negative rods would likely predominate. However, the results obtained by culture (Table V) indicate that comparatively few of the types of organisms belong to this group. No particular effort was made to identify those organisms not of the colon group, as it had been considered that only the latter are commonly associated with clinical infection.

TABLE V

ORGANISMS	ANTEPARTUM PATIENTS		POSTPARTUM PATIENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
No growth	32	21.2	22	14.7
<i>Escherichia coli</i>	9	6.0	8	5.3
<i>E. communior</i>	4	2.7	9	6.0
<i>Alcaligenes fecalis</i>	6	4.0	5	3.3
<i>Bacillus subtilis</i>	6	4.0	6	4.0
<i>Staphylococcus albus</i>	12	8.0	20	13.3
Monilia	7	4.7	1	0.7
Gram-positive rods	16	10.7	7	4.7
Miscellaneous	58	38.7	72	48.0
	150	100.0	150	100.0

Cultures indicate a greater number of specimens to be bacteria-free, as measured in terms of ability to grow and form colonies, than is shown by the study of stained slides of urinary sediment. Both methods, however, demonstrate that very few of these specimens, even though obtained by catheterization, were sterile. The presence of certain organisms, *Staphylococcus albus* and *Bacillus subtilis*, suggest contamination during or after catheterization, while some of the unidentified, gram-positive rods may have been the vaginal bacilli of Döderlein.

It is apparent (Table VI) that increased numbers of cells per high power field were, in general, paralleled by a greater incidence of

pyelitis, but 27 per cent of antepartum and 24 per cent of postpartum women with marked pyuria (more than 50 pus cells per field) had no associated clinical evidence of pyelitis. Also, 5 of the 10 patients showing 200 or more pus cells per field were free of urinary symptoms, whereas one antepartum woman had symptoms of pyelitis with less than 5 cells per field.

TABLE VI. THE RELATION OF PYURIA TO CLINICAL MANIFESTATIONS

AVERAGE NUMBER OF PUS CELLS PER HIGH POWER MICROSCOPIC FIELD	ANTEPARTUM PATIENTS			POSTPARTUM PATIENTS				
	NO. OF CASES	PYELITIS		NO. OF CASES	PYELITIS		FEBRILE PUERPERIUM	
		NO.	PER CENT		NO.	PER CENT	NO.	PER CENT
0 to 5	86	1	1.2	66	0	0.0	13	19.7
6 to 10	12	0	0.0	22	0	0.0	2	9.1
11 to 25	16	0	0.0	19	1	5.3	4	22.2
26 to 50	14	2	14.3	18	0	0.0	3	16.7
51 to 100	6	1	16.7	12	3	25.0	3	25.0
101 to 200	9	2	22.2	10	1	10.0	3	30.0
More than 200	7	3	42.9	3	2	66.7	2	66.7
	150	9	6.0	150	7	4.7	30	20.0

DISCUSSION

These data indicate that moderate numbers of pus cells are a normal finding in the urine of women during late pregnancy and the early puerperium. Pyuria, then, does not necessarily mean that the patient has pyelitis, nor does its absence eliminate the diagnosis of this clinical entity. It is possible that the pain and tenderness over the kidney region in patients with pyelitis are due to distention of the renal pelvis, and that this may or may not result in the exudation of polymorphonuclear cells into the urinary tract. The function of this tract, having thus been interfered with by the distention producing factor, may become secondarily invaded by a number of organisms. These latter may then be considered incidental to the essential lesion, but may contribute somewhat to the disturbance of function. An analogous condition is found in the secondary invasion of the bladder by bacteria when there is some interference with normal emptying. If this is accepted, it is apparent that the chief distinctive evidence of urinary tract infection is the discomfort incident to the accompanying cystitis and to the fever with chills.

CONCLUSIONS

1. Bacteria and pus cells are present in the urine of practically all late pregnant and early puerperal women but are without clinical significance in themselves.
2. The diagnosis of pyelitis must rest on symptomatology and may or may not be accompanied by pyuria and bacteriuria.

CERVICITIS AND ENDOCERVICITIS IN RELATION TO GYNECOLOGIC SYMPTOMATOLOGY*

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THE consideration of cervicitis and endocervicitis probably seems a very elementary problem. However, when one constantly sees patient after patient presenting themselves for relief of various gynecologic complaints, and have been advised to have major surgical procedures done for the relief of these symptoms, one is inclined to stop and wonder if we are not frequently overlooking a very simple and common cause of these complaints, namely, inflammatory lesions of the cervix and endocervix.

Cervicitis and endocervicitis are such extremely common conditions that we are inclined to disregard their major importance in gynecologic symptomatology. Briefly, reviewing the etiology of cervicitis and endocervicitis, we find that it is most often found in women who have had one or more children with resulting lacerations in the cervix, permitting easy access of bacteria into the cervical canal. It is not at all uncommon, however, in nulliparous women, young girls, and even in infants. It is a question whether the cervix ever escapes contamination in ascending infections of the genital tract. Infection once implanted on the cervical mucous membrane may endure for an indefinite period of time due to the anatomical construction of the endocervix, particularly because of the folds of the cervical mucosa and presence of compound racemose glands. Infections in this region may be deep seated, which fact explains the difficulty in curing these lesions and the tendency to chronicity. Inflammatory reaction and infection of the cervix is usually brought about by lacerations, exposure to sex trauma, instrumentation, and its being constantly bathed in bacteria of one type or another, thus introducing the infection into the cervical canal. As a result of these infections numerous symptoms may develop depending upon the severity and extent of invasion and involvement of the reproductive organs.

Leucorrhea is probably the most common symptom resulting from bacterial invasion of the endocervical glands. This discharge may in turn produce changes in the vulva not unlike that seen in diabetes, leucoplakia, and kraurosis vulvae. The associated symptoms are those of burning, intense itching, smarting on urination, and dyspareunia.

*Read at a meeting of the Chicago Gynecological Society, January 17, 1936.

Similar symptoms may be produced by a vaginitis as a result of various organisms, the most common of which are *Trichomonas vaginalis*, streptococci, yeast and fungoid infections, all of which may have an associated cervical infection. Satisfactory results in the treatment of many of these cases are not obtained until the cervical infection is eliminated. In infants and young girls the discharge and vaginitis produced by endocervicitis and cervical erosions are not infrequently mistaken for a specific infection. Cervical lesions causing leucorrhea are also one of the most common causes of relative sterility, mainly, by blocking the entrance of sperms into the uterine cavity. It may also change the character of the bacterial flora and conditions in the vagina which either actively prohibit the motility of the sperms or noticeably retard their activity.

The cervix is richly supplied with lymphatics which combine with the lymphatics of the upper part of the vagina and drain into the iliac glands. This may produce marked induration of the uterosacral ligaments causing them to be extremely swollen and tender, producing pain and backache in the sacral and lumbosacral regions. This backache may be in part reproduced by touching the inflamed cervix with a strong chemical irritant such as tincture of iodine or silver nitrate. Many times the patient will say that this procedure reproduces the exact pain for which she presents herself for relief. The pain can also be reproduced by pushing the cervix anteriorly, putting the uterosacral ligaments on a stretch. Induration and tenderness of the uterosacral ligaments also often produce dyspareunia.

Burning on urination, urgency, and bladder tenesmus are occasionally found to be relieved by clearing up an existing cervical lesion. Whether these bladder symptoms are due to direct infection through the urethra or by lymphatic drainage is problematical.

There are many patients who present themselves with symptoms of sacroiliac arthritis or subluxation, which promptly disappear after clearing up any existing cervical infection. As evidence of this I would like to present a typical case history.

Mrs. H., aged twenty-eight, came in to see me June 10, 1935, because of an irritating profuse leucorrhea which she had had since the birth of her child eighteen months previously. She also complained of dyspareunia and a severe sacral backache during this time which had been diagnosed as sacroiliac arthritis for which she had had a tonsillectomy done and two teeth extracted. She was told that she had a retroverted uterus that would need surgical correction. She also had been under the care of an orthopedic surgeon who prescribed a body cast which she had worn for about six months, removing it temporarily for physiotherapy and massage. None of the foregoing management had given relief. On examination the patient had a moderate cystocele and rectocele. There was a profuse mucopurulent discharge in which no *Trichomonas vaginalis* could be found. The cervix was edematous, lacerated bilaterally, badly eroded and contained several infected nabothian cysts. There was marked induration and tenderness of both uterosacral ligaments. The uterus was retroverted, enlarged, and tender on motion, no abnormal masses could be

felt in the region of either adnexa. Pushing the cervix anteriorly reproduced the pain in the back, of which she complained. The cervix was cauterized on three different occasions, the nabothian cysts destroyed with the fine pointed cautery. At her last visit November 5, there was no leucorrhea, the cervix was clean, uterus in normal position, and she was free of all backache and pelvic discomfort.

The increased size and boggiess of the uterus due to inflammatory lesions of the cervix is frequently the cause of retrodisplacements, the uterus falling back because of its increased size and weight. On the other hand, there are many cases of retroverted uteri producing symptoms of pressure in the pelvis, backache, dysmenorrhea, dyspareunia, and leucorrhea that are thought to be due to the position of the uterus. These symptoms often disappear after existing cervical lesions are cured, even though the uterus remains retroverted, thus proving that it was not the retroversion that was causing the trouble but the associated cervical infection. These retrodisplacements may spontaneously return to normal position when the existing cervical infection is relieved. This is particularly true of retroverted uterus with cervical lesions following childbirth.

There is some argument as to whether cervicitis and endocervicitis can act as a focus of infection. There are some who claim that this is true and that an infected cervix is analogous to the tonsils, teeth, or other foci. There are others who say that infections in the cervix never act as a general systemic foci, causing arthritis, neuritis, neuralgia, etc., except gonorrheal infections which may cause gonorrheal arthritis. However, it is not inconceivable that some cervical infections may be related to general systemic or rheumatoid conditions.

Endocervicitis, cervicitis, erosion, ectropion and polypus formation all are related conditions and may represent different stages of the same process. Erosion, ectropion and cervical polyps may, and frequently do, produce contact bleeding and metrorrhagia not unlike that seen in malignancy. The appearance is frequently very similar and cannot easily be differentiated. Senile atrophy sometimes predisposes the endocervix to infection producing partial or complete atresia. The result may be the backing up of infection in the uterine canal, producing a pyometra which is thought to be an etiologic factor in the production of malignancy of the corpus.

Severe dysmenorrhea may also be an associated symptom especially when an erosion is present. Many women have had a dilatation and curettement done for dysmenorrhea with no relief until existing cervical lesions are eradicated.

Menorrhagia or increased duration and quantity of menstrual flow, not infrequently mistaken for that caused by fibromyoma uteri, is in reality often the result of an inflammatory process secondary to cervicitis and endocervicitis.

As an example of this I would like to present another case history. Mrs. K., aged forty-three, presented herself Sept. 26, 1932, complaining of pain and dragging sensation over the right inguinal region, profuse menstrual periods, lumbosacral backache, and severe dysmenorrhea. Menstrual history: Onset at twelve, regular, twenty-eight-day interval lasting three or four days, with use of 6 or 8 napkins during the period, and no pain. For the last year the periods had gradually come to last seven or eight days and become more profuse, requiring 18 to 24 napkins, with pain lasting throughout the entire period and much generalized discomfort. During this time she also had noticed a moderately profuse vaginal discharge. She had one miscarriage, two children the youngest being 14 years. Vaginal examination revealed a moderate cystocele and rectocele. The cervix was lacerated bilaterally, edematous, filled with nabothian cysts and badly eroded. The uterine ligaments were tender and indurated. The uterus was in normal position about the size of a small orange, boggy in character except for a fibroid nodule in the right horn about the size of a large English walnut. The patient was told that her difficulty might be in part caused by the infected lacerated cervix and in part by the fibromyoma. She was advised to have the cervix cleaned up before any operative procedure that might be necessary. I did not see the patient again for about two months during which time she had visited one of the better clinics where she was told that she had a fibroid the size of a grapefruit and an immediate hysterectomy was advised. She again presented herself for attention and the cervix was cauterized on four different occasions. At the time of her last visit, Sept. 3, 1935, the uterus was definitely smaller in size. The fibroid had not increased in size and she was free from backache, dysmenorrhea, and leucorrhea. The last three periods had been at twenty-eight-day intervals, lasted three or four days and required 8 or 9 napkins during the entire period. This case proves beyond question that the cervical lesion was responsible for her complaints rather than the existing fibromyomas.

700 NORTH MICHIGAN AVENUE

DISCUSSION

H. O. MARYAN.—I wish to report the results of 32 cases of urinary disturbance due to chronic cervicitis. This work was done in collaboration with Drs. Russel Herrold and E. Ewert of the Urological Department of the University of Illinois. The method of treatment in all these cases was electrical coagulation by means of the crucial incision and stripping method.

These women generally complain of frequency of urination with burning before and after, intermittent deep pain above the pubis, low backache, and less frequently, radiating pains into the groin, the thigh, and upward along the course of the ureter. This syndrome is frequently designated as the irritable bladder, some believing the urine to be bacteria free. Many of these patients have pronounced leucorrhea.

DR. HOLLOWAY (closing).—I have had two patients with persistent bladder symptoms in spite of a urine in which pus was never noted. Urethral polyps were found and removed but the symptoms continued. The patients subsequently became symptom free after cauterization of the cervix.

Some of these cervical glands may extend up to the uterine body. Cauterization to the level of the internal os would not, therefore, remove all the potentially infectious gland tissue.

SYMPTOMATIC RUPTURE OF THE GRAAFIAN FOLLICLE OR CORPUS LUTEUM

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THE rupture of a graafian follicle and the development of the corpus luteum, although usually unattended by untoward symptoms, may on occasion be the cause of severe abdominal complaints. The condition is seldom recognized before operation since the symptoms closely resemble those produced by other pelvic or gastrointestinal diseases.

A review of the literature by Morton¹ in 1932 revealed 93 authentic cases. Since then additional cases have been added to bring the number well over one hundred.²⁻⁴ Most reported cases present marked and sometimes alarming symptoms of severe hemorrhage from the follicular apparatus. These are characterized by severe sudden pain, which is likely to be lower abdominal at first, but which may later become generalized, and also by evidence of hemorrhage, such as rise in pulse, fall in blood pressure, pallor, faintness, nausea, and /or vomiting.

More recently Pratt⁵ placed emphasis upon the development of mild or moderate symptoms associated with ovulation and the formation of the corpus luteum when there was little or no hemorrhage from the ovary. He pointed out that a thorough familiarity with these symptoms is essential in differentiating between this condition and appendicitis.

From the material available at the University Hospital and the Chicago Lying-In Hospital, we are able to analyze 17 cases and the findings are summarized here.

The youngest patient was seventeen and the oldest forty years of age, with an average age of twenty-six years. There were 7 multiparas and 10 nulliparas. Fifteen of the patients gave a normal and regular menstrual history while one patient menstruated every six to eight weeks, and one, although presenting well-developed secondary sex characteristics, had never menstruated.

Pain was the only constant symptom in all cases and was the first symptom in each. Its severity varied from a mild, dull ache to very severe pain causing fainting. In every instance the onset was sudden. Eight patients had pain only in the right lower quadrant, 3 in the left lower quadrant, and 6 complained of generalized lower abdominal pain. Eight complained of nausea and vomiting, while the remaining 9 had no gastrointestinal symptoms. In previous reports trauma has been mentioned as an important etiologic factor. In this group there was a record of trauma in only 2 cases. One patient developed symptoms immediately after a vaginal examination and the other during rather strenuous exertion (running).

The time of onset of the symptoms in relation to the cycle is of interest in differentiating between follicular and corpus luteum hemorrhage (Table I). Five of the patients developed their symptoms from thirteen to fifteen days after onset of the previous period. Material for microscopic study was available in 4, and, in all, revealed only cystic follicles with hemorrhage. The other patient was treated con-

servatively and was discharged in three days. Ten patients developed symptoms later than three weeks after the previous period. Pathologic material from these showed large corpora lutea with hemorrhage. The other 2 patients had irregular and atypical menstruation, and the time of onset in relation to the period was questionable, but in each it was more than three weeks after the previous period. Both of these patients were found to have hemorrhage from a corpus luteum.

Physical examination in this group of patients gave very few consistent findings. Lower abdominal tenderness either general or limited to one of the lower quadrants and of varying severity was present in all cases. Muscle spasm over the side involved was present in about one-half of the cases. Three patients did not have a pelvic examination. Pelvic examination in the remainder revealed tenderness on manipulation of the uterus in all cases. A definite mass was felt in the region of the involved appendage in 5 cases. In 4 an indefinite mass was noted, while in 5 no mass could be palpated.

TABLE I. ONSET OF SYMPTOMS IN RELATION TO CYCLE

MENSTRUAL PHASE	PROLIFERATIVE PHASE	OVULATION TWELFTH TO SIXTEENTH DAY	PREMENSTRUAL PHASE
1-1 Day after onset		2-13 Days postmenstrual	1-21 Days postmenstrual
1-3 Days after onset		3-14 Days postmenstrual	1-22 Days postmenstrual 2-27 Days postmenstrual 2-28 Days postmenstrual 1-29 Days postmenstrual
All showed hemorrhage from corpus luteum		All showed hemorrhage from graafian follicle	All showed hemorrhage from corpus luteum

Two cases with grossly irregular menstrual history had hemorrhage from a corpus luteum. One patient treated conservatively. Pathologic material not available for study.

The temperature varied from normal to 101°. The higher fevers occurred in the patients with higher leucocyte counts. The pulse was slightly elevated in about one-half of the cases, with an average pulse rate of 88.

The leucocyte count varied from 5,400 to 22,650. The degree of reaction in the blood corresponded roughly to the time interval between the hemorrhage and the examination, and to the amount of organization of the hematoma which had taken place, i.e., the lowest counts were in those patients with fluid blood or follicular fluid in the abdomen who were seen a few hours to one or two days after the onset of symptoms. The higher counts occurred in those patients seen a week or more after onset. The count of 22,650 was in a patient whose symptoms had persisted for five weeks.

The original diagnoses (made when the patients were first seen) were as follows: In 5 the diagnosis was ectopic pregnancy. Seven were diagnosed appendicitis, 1 a hydrosalpinx, and 1, the patient with total primary amenorrhea, was thought to have an ovarian neoplasm with some degenerative change. Three patients were diagnosed as ruptured follicle with hemorrhage, and in one of the cases which was diagnosed as appendicitis, the possibility of rupture of follicle with hemorrhage was mentioned. One of the patients with the original diagnosis of ruptured follicle was not operated upon, but in view of the convalescence and future course, we felt justified in including the case in this report.

At the time of operation 15 of the 16 patients showed gross blood in various stages of organization. The other patient presented a rent in the surface of the right ovary with a small hematoma in the follicle and a small amount of clear fluid in the culdesac. The occurrence of symptoms in the presence of gross hemorrhage is understandable. The presence of symptoms in the one case without hemorrhage, however, leads us to agree with Pratt that the rupture of the follicle with discharge of follicular fluid is capable of producing sufficient peritoneal irrita-



Fig. 1.—Photomicrograph from case of follicular rupture with hemorrhage showing granulosa cells, ovarian stroma and extravasated blood. ($\times 65$)



Fig. 2.—Photomicrograph from case of corpus luteum hemorrhage showing lutein cells, ovarian stroma and hemorrhage. ($\times 63$)

tion to cause clinical symptoms, and has caused us to be more careful when investigating female patients with symptoms of acute appendicitis.

The differentiation cannot always be made but a consideration of the salient points will be helpful. The onset of the pain in follicular rupture usually is more sudden and sharp and starts over the area involved. Nausea and vomiting are less pronounced; temperature and leucocyte count are usually lower. The localization of tenderness is below McBurney's point (Table II).

TABLE II. DIFFERENTIAL DIAGNOSIS

SYMPTOMS	APPENDICITIS	FOLLICULAR RUPTURE
Pain	Starts in epigastrium then localizes in the R.L.Q.	More sudden and severe. Starts over involved appendage
Tenderness	Maximum at McBurney's point	Maximum apt to be below McBurney's point if in right side
Leucocytes	10,000-15,000	Normal or only slightly elevated in mild cases
Fever	Normal—101	Seldom over 100°
Nausea and vomiting	The rule	Less common except in more severe cases
Menstruation	No definite relation to cycle	Variable but usually either at time of ovulation or premenstrual or early menstrual phase

The question of operation should depend on evidence noted in each case. In any event, operation is indicated regardless of the differential diagnosis when symptoms indicate a major abdominal crisis.

SUMMARY

The sudden onset of lower abdominal pain in any woman at the time when ovulation should occur (twelve to sixteen days postmenstrual) or shortly before the onset of menstruation, with or without slight fever and leucocytosis, suggests the diagnosis of ruptured graafian follicle or corpus luteum. The severity of the symptoms should be the guide in regard to operation. If mild, observation for a few hours with frequent check of the fever and leucocyte count and close observation of the patient for evidence of progressive hemorrhage is indicated. If the possibility of appendicitis cannot be satisfactorily ruled out and operation is decided upon, we favor the use of a median or paramedian incision to permit adequate exploration of the pelvic viscera.

The treatment of the ovary at the time of operation will depend entirely upon the amount of pathologic change present. In the case of a small rent with mild hemorrhage, suture of the opening is adequate. In the presence of larger hematoma partial resection of the ovary may be necessary, and when the whole appendage is involved with organizing hematoma, it may be wise to remove completely the involved tube and ovary.

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DÜHRSSSEN'S INCISIONS*

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INCISION of the cervix as an aid to delivery is on record as early as the eighteenth century, but it was Dührssen who showed the value of these incisions so conclusively. The usefulness of this operation is limited to some extent because incision is safe only after effacement of the cervix. Dührssen proposed deep lateral incisions and if not sufficient, anterior and posterior as well. Recent reports on the use of cervical incisions indicate that at present they mostly are made in the oblique diameters, which seem to be preferable. Available records indicate that these incisions are used as a last resort after long difficult labors without advancement of the head.

I am not advocating anything new as to procedure, which is very simple, but I am pleading for more frequent use of the incisions in definitely indicated conditions, which I shall take up later.

Shir† in a rather apologetic manner states that he does not wish to be understood as advocating frequent Dührssen's incisions of the cervix. Quite to the contrary he looks upon it as a major operation to be resorted to but rarely though there is a definite field for its occasional use. He feels that conservative waiting beyond a certain point is no longer a virtue.

Shir reports the type of case known to all obstetricians. Labor goes on hour after hour, sometimes several days; finally the cervix disappears, the occiput rotates, and the baby may be delivered. These patients, however, later show a deep bilateral laceration of the cervix into the vault of the vagina. What has taken place is not dilatation at all, but gradual edema and loss of elasticity of the cervix with finally spontaneous laceration. I readily agree with Shir when he states that to push the cervix back over the head is simply to lacerate it instead of incising it. His records show that incisions were made once in every 161 cases. The average stay in the hospital was 15.8 days in spite of the fact that labor usually lasted over two days, showing that morbidity was not great. This operation was resorted to in his series only after a long labor when the patient was already infected and worn out, and the baby was in grave danger. Twenty-seven of these 143 babies were lost, 6 of these were dead before interference was attempted.

*Read at the Seventh Annual Meeting of the Central Association of Obstetricians and Gynecologists, held at Omaha, Neb., October 10 to 12, 1935.
J. AM. J. OBST. & GYN., 26: 425, 1936.

Such figures might indicate that Dührssen's method is risky and objectionable. However, I desire to show that had Dührssen's method been applied earlier in labor many of these babies might have been saved.

Caldwell, in Curtis' *Obstetrics and Gynecology*, states that attempts to deliver through the obstructed cervix without incision leads to spasms of the lower uterine segment, and that many of these patients can be delivered easily after cervical incision, saving the baby and leaving the mother in a better condition. Incisions are more easily repaired and heal better than ragged tears.

Given a fairly normal pelvis and a child not out of proportion, the most frequent cause of delayed difficult delivery is the occipitoposterior position. Fetal mortality and maternal injury and morbidity in these cases is still too high. Many methods have been advocated for their management. Although it is recognized that various types of pelvic disproportion are causes of occipitoposterior positions, there are many cases which are not explained by abnormal pelvis. The etiologic factor here probably lies in the uterus or the cervix. It is usually in this type of case, where advancement and rotation fails to take place and the cervix does not dilate beyond four fingers, that I advocate more frequent and earlier use of incisions of the cervix. Although incisions may help in some of these other cases, I do not consider it justifiable to employ them as frequently as with the normal pelvis, since other factors must first be evaluated. The by-word of all obstetrics is watchful expectancy, in other words, as far as possible, conservatism. When progress is definite and mother and baby are in good condition, I am sure everyone agrees that this is by far the best policy. However, in the type of cases under discussion, where the cervix does not dilate properly and progressively, but with the continuation of labor the edges become thicker and more edematous, I have obtained by far the best end-results as to both mother and child by what might be considered a radical procedure but which I believe to be conservative.

In going over my records and examining the patients for end-results I have found that those patients who were allowed to labor for many hours, with a thick cervical rim, almost invariably showed deep bilateral lacerations, frequently into the vault of the vagina. After patient waiting we suddenly find that we seemingly have been rewarded and the baby is born. The end-results prove that this was not a conservative procedure, as the fetal mortality is high and maternal damage is great. On the other hand, in this type of case where the cervix dilates to three or four fingers and remains stationary for two

or three hours, the head failing to advance or to rotate, incisions usually terminate labor very quickly with both the baby and the mother in better condition.

I have found that in the majority of these cases two incisions in the position of ten and two on the clock are sufficient if the incisions are made at least $1\frac{1}{2}$ to 2 inches long. The surprising feature is the exceedingly small amount of bleeding; often no blood loss at all being encountered, probably because of the extreme edema and anemia of the cervix at the time of incision.

Repair of the cervix is exceedingly simple even without special retractors, as the cervix can easily be pulled down with sponge forceps. Two interrupted sutures, as a rule, in each incision is all that is necessary. The follow-up after six or eight weeks has shown normal appearing cervixes, sometimes requiring close search for the scar of the incision.

Although I realize that this series consisting of 36 cases is small, the results have been so entirely satisfactory that I feel I can draw some definite conclusions. In fact, the corrected fetal mortality of this series is zero. There were three dead babies. Two of them were cases of craniotomies for hydrocephalic and exceedingly large babies, their heads being almost the size of watermelons. The other death was that of a 1,600 gm. baby with multiple anomalies, born alive, dying later. A few case reports follow to show the types of labor with the results, which allow me to draw my conclusions.

The first few cases of the series showed a longer labor than did the cases of the last few months. In these I have taken a more positive stand and have terminated labor earlier when dilatation and advancement of the head had apparently ceased.

The first case of this series occurred about four years ago. This primipara entered the hospital with ruptured membranes, contractions every two minutes, of sixty to seventy seconds' duration. Position was R.O.P. and the cervix effaced and one finger dilated. Dilatation was rather slow from the start, and after seven hours of labor in the hospital, she had only two and one-half fingers' dilatation. Fourteen hours later she had three fingers' dilatation with the head still in midpelvis and the occiput posterior. Three hours later this patient had four and one-half fingers' dilatation. This was after a labor of almost twenty-four hours. Four hours later this patient still had four and one-half fingers' dilatation, the head was still in midpelvis and the anterior lip was becoming markedly edematous. Two hours later as conditions were still the same, the patient was given an anesthetic and Dührssen's incisions were made in the position of ten and two on the clock. Mid-forceps Scanzoni maneuver was done without difficulty and the patient delivered after an episiotomy. Repair of the cervix was accomplished with two interrupted No. 1, twenty-day catgut sutures on each side. The perineum was repaired and the postpartum course was normal. This labor lasted over thirty hours with a baby weighing only 2,550 gm. and with a normal pelvis. Examination of the cervix six

weeks later showed it to be normal without eversion and genitalia in good condition. Delay of labor in this case was due primarily to the cervix and the posterior position was secondary.

There were three cases of breech presentation in this series which were delivered without difficulty after Dührssen's incisions were made. All were primiparas. Two of them showed no progress after four to four and one-half fingers' dilatation with the breech in midpelvis, contractions being good. The first patient was allowed to labor ten hours without progress before incisions were made. The second case was delivered following incision of the cervix when labor showed no progress after four hours. The third patient had one finger dilatation on entrance to the hospital. Labor was satisfactory and progressive with four fingers' dilatation six hours later. At this time the membranes ruptured spontaneously and on examination a prolapsed cord was found. Fetal heartbeat was 80 per minute. A living baby was delivered here also following Dührssen's method. All of these patients had three incisions as I wished to be certain that the cervix would not interfere in any way with the aftercoming head.

There was one case of twins in a very small woman, weighing 91 pounds when she first came to see me and 124 pounds at the time of delivery. McDonald measurement was 46 cm. The abdomen was so large that the labor pains although frequent and of good quality were ineffectual. Although pains were almost continuous for about four hours before the patient was placed on the delivery table, there was no progress in dilatation. Examination revealed four fingers' dilatation from 7:30 P.M. to 11:50 P.M. At this time two incisions were made in the cervix, the anterior lip of which was becoming edematous, and both babies delivered without difficulty. Delay in these cases was probably due to insufficient uterine force.

Twenty-eight patients of this series were primiparas and eight were multiparas.

One multipara had a three-hour labor with the first baby and no difficulty. With this second child the position was R. O. P., pains good, every two minutes, of sixty to seventy seconds' duration. This patient had four fingers' dilatation after twelve hours in the hospital with hard contractions. Two hours later there was still four fingers' dilatation and the membranes were ruptured artificially. Three hours later, with good cooperation from the patient there was no further advancement and the anterior lip was very edematous. The patient was tired. She was placed on the delivery table and two Dührssen's incisions were made. Four minutes later after two contractions the head was found on the pelvic floor and delivered with perineal forceps.

Two other patients, primiparas, were allowed to deliver spontaneously after the incisions were made. These patients had been in active labor for several hours without progress after four fingers' dilatation. The head could be seen to rotate and descend with the first pain after the incisions. These patients both delivered spontaneously without difficulty. These cases proved to me that occiput posterior was secondary and the cervix primary.

The two patients with hydrocephalic babies, both primiparas, had labors somewhat similar, lasting more than forty-eight hours, with irregular ineffectual contractions. Dilatation was two fingers at this time, and a bag was inserted into the cervix. The bag was expelled after several hours with about four fingers' dilatation. Contractions again became irregular and the cervix contracted down to about two and one-half fingers. During this time the patients had been given morphine and hyoscine at intervals, as well as intravenous glucose. As there was complete effacement, three Dührssen's incisions were made, and the babies were delivered after craniotomy.

One patient in this series had Dührssen's incisions for both deliveries, both labors being similar with primary inertia and no progress after about three fingers' dilatation. Two other primiparas who had Dührssen's incisions with the first delivery have since been delivered spontaneously after short normal labors.

At the present time after observing these patients and comparing them with other cases of retarded labor, I feel very definitely that it is not a radical procedure to make these incisions in the cervix, when after three or four hours of good labor there is no advance of the head or appreciable increase in dilatation of the cervix. There was no maternal mortality and the morbidity was no higher than that following normal cases. The end-results have been consistently good. On the other hand, in patients in whom the policy of watchful expectancy had been followed, the cervixes showed deep bilateral lacerations and the end-results were not so good. The total number of deliveries during the four-year period of this report was 583; or 6 per cent had Dührssen's incisions.

CONCLUSION

1. The performance of Dührssen's incisions is a safe and simple operation but must be done after complete effacement when the vessels and bladder are well retracted. If there is no effacement, Dührssen's incisions should not be done.

2. The type of case in which this operation is most satisfactory is the one in which the patient has been allowed to go spontaneously into labor because of normal pelvic measurements, and in whom the progress is not satisfactory because of malposition or inertia or abnormality of the cervix, and particularly, where the membranes have been ruptured, when it would be more hazardous to attempt cesarean section.

3. I am not suggesting any change in Dührssen's method but I am advocating a much earlier and more frequent use of the method in properly selected cases, as I am certain that it is the means of saving many babies who would otherwise be lost.

1027 MISSOURI THEATRE BUILDING

Vayrynen, V.: Cases of Polyneuritis and Myelitis Caused by the Toxemias of Pregnancy, *Acta obst. et gynec. Scandinav.* 15: 182, 1935.

The author reports 5 personal cases of myelitis and polyneuritis caused by the toxemias of pregnancy. The clinical picture of these cases was the same as it is for these diseases in the nonpregnant state. The disease usually begins as ordinary vomiting of pregnancy. It soon becomes excessive vomiting. Hence, in all patients who have hyperemesis gravidarum the nervous system should be carefully investigated. Because of the high mortality (42 per cent), the author advises interruption of pregnancy as soon as any signs of paralysis appear.

J. P. GREENHILL.

TRIPLE PREGNANCY DIAGNOSED BY MEANS OF X-RAY

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A CAREFUL search of the available literature reveals only 9 cases in which the diagnosis of triplets was made before delivery. H. Marcus¹ reviewed the literature in 1928 and found 4 cases to which he added a fifth. To briefly summarize Marcus' report: Edling² reported a case in 1911 in which the diagnosis of twins was made by x-ray at the fourth month. The patient delivered triplets and, upon reexamining the plates, shadows which were not noted before delivery were interpreted as being those of the third fetus. Essen-Möller³ in 1920 had a patient delivering triplets on whom an x-ray examination was made before delivery but after she had started into labor. The diagnosis was made at the time of delivery before the result of the examination was known. Favreau and Despons⁴ in 1924 made a diagnosis of triplets by x-ray at the sixth month. Genell⁵ in 1926 diagnosed a triple pregnancy by the visibility of 3 vertebral columns on the x-ray film. Marcus' patient was a primigravida, twenty-nine years old, who was first seen about two weeks before the expected date of confinement. Her abdomen was very large, and it was difficult to make an exact examination because of the tenseness of the abdominal wall. There were 2 resistant surfaces felt which gave the impression of backs. A fetal heart could be heard distinctly at one point. When the patient returned one week later, examination by palpation was no more satisfactory than at the first visit, and it was decided to make an x-ray examination. The membranes ruptured spontaneously the same evening and she started into labor. The results of the x-ray examination were made known during the course of labor and indicated a triple pregnancy. Two of the fetuses were well developed, but the bones of the third seemed to be lying in an irregular-shaped mass, indicating that the fetus was dead and macerated. The accuracy of the radiologic diagnosis was confirmed at delivery.

Dr. Robert A. Johnston⁶ also, in 1925, reported a case of triplets diagnosed by x-ray two months before delivery. Two fetal hearts had been heard but a definite diagnosis by palpation was not possible. The patient was delivered approximately at term of 3 living children. A recent letter from Dr. Johnston states that they are still living and in excellent health.

There were 2 cases reported in 1930. Dr. Leo A. Rowden⁷ reported the diagnosis of triplets by means of the x-ray one month before delivery. The patient was delivered of 3 healthy male infants at the seventh month. The writer makes the statement that he has not seen another case in the English literature. Trillat, Eparvier, and Naussac⁸ reported the case of a thirty-year-old primigravida who was first seen at term. The abdomen was very large, measuring 44 cm. vertically. The first examination indicated a twin pregnancy but repeated examinations revealed a mass just below the umbilicus which might have been a fetal head. An x-ray examination showed the presence of 3 fetuses. The authors stressed the fact that a correct diagnosis could have been made only by x-ray, as diagnosis by palpation alone was impossible. The labor was long with mild infrequent pains. Delivery was completed under general anesthesia and 3 living infants were extracted. All 3 children lived.

The ninth case was reported by Dr. Albert H. Aldridge⁹ in 1932. The diagnosis was made three weeks before the expected date of confinement by means of the x-ray.

All 3 babies were breech presentations. The patient went into labor two days later and delivered the first baby spontaneously at the end of the second hour. The other 2 babies were easily delivered. The delivery was uncomplicated, except that immediately postpartum the patient had a rapid rise in pulse rate to around 200 per minute. It fell abruptly after twenty-five minutes to 80 per minute and remained normal. The puerperium was uneventful. All 3 babies were males and were born alive; their weights were 4 pounds 7 ounces, 4 pounds 3 ounces, and 3 pounds 3½ ounces, respectively. The oldest and largest child died at four months of gastroenteritis but the other 2 were living and well at the time the report was made. There were 3 separate placentas and fetal sacs.

The case which I wish to report is similar to those previously reported, in that the correct diagnosis was not made without the aid of the roentgenologist. That this aid in diagnosis is being used more frequently as time goes on is illustrated by the fact that 5 cases were reported before 1930 and 4 since that time. It seems reasonable to presume that, in the future, the presence of triplets will be recognized more often before delivery by the use of this valuable method of examination.

CASE REPORT

Mrs. M. T., white, aged twenty-three years, para 0-0-0-0 was first seen on Sept. 9, 1935, having been referred by her family physician for prenatal care and delivery. Her father died of "a fever and asthma" and her mother following "a stroke." The family history was otherwise negative. There was no history obtainable of multiple pregnancy in the family of either the patient or her husband. The patient's past history was negative except for tonsillectomy one year ago for hypertrophied tonsils.

Menses began at the age of fourteen years and were always regular every twenty-eight days, lasting three days with slight pain. The last period began May 5, 1935, making the estimated date of confinement Feb. 12, 1936. She had had some nausea and vomiting associated with slight headaches early in her pregnancy. There had been no edema or bleeding. Her bowels were regular, but she complained of hemorrhoids which gave her some discomfort at times. Fetal movements had not been felt. She stated that her general health was excellent and that she felt well.

Examination: Head and neck were negative, lungs clear, heart sounds normal. Breasts were well developed and contained colostrum. The abdomen was negative except for the enlarged uterus which seemed larger than the period of gestation would indicate. Height of the fundus uteri from the symphysis pubis was 18 cm. and estimated duration of pregnancy was twenty-four to twenty-six weeks. The position of the fetus could not be determined and the fetal heart could not be heard. Pelvic measurements were within normal limits, blood pressure 110/70, weight 107 pounds. Patient said her usual weight was around 90 pounds. Urinalysis showed nothing abnormal. On October 18 the blood pressure was 120/80, weight 116½ pounds, height of the fundus uteri 23 cm. It was still impossible to determine the position of the fetus and the fetal heart could not be heard although the patient said she felt movements. Moderate hydramnios was noted at this time, but in spite of the abnormal tension of the uterus and the rather rapid distention of the abdomen, the patient said that she felt well and was able to walk long distances without tiring. On November 1 the height of the fundus had increased to 28 cm., the circumference of the abdomen at the level of the umbilicus was 80 cm., and there was more tenseness from the increased hydramnios. Her weight at this time was 120½ pounds. Because the hydramnios had increased so markedly, and it was still not possible to palpate the fetus, a roentgen examination was decided upon to determine, if possible, the presence of twins or a monstrosity. At this time a ballotable mass could be felt just above the symphysis and a fetal heart could be heard about the level of the umbilicus and 3 cm. from the midline

on the left. The roentgenologist reported on November 4 that the examination revealed the presence of triplets, the first fetus presenting by the occiput with the back to the right, the second as a transverse presentation with the head to the left, and the third as a breech presentation with the back to the left.

An attempt was made to control the hydramnios by limiting the fluid intake, and a careful fluid record was kept until the date of delivery. At no time was there more than a normal variation between the fluids taken in and those excreted. Whether the hydramnios decreased or not is open to question. However, it can almost be said with certainty that it did not increase. During the five and one-half weeks between the time of diagnosis of multiple pregnancy and delivery, fetal parts gradually became palpable but at no time was it possible to outline a single fetus

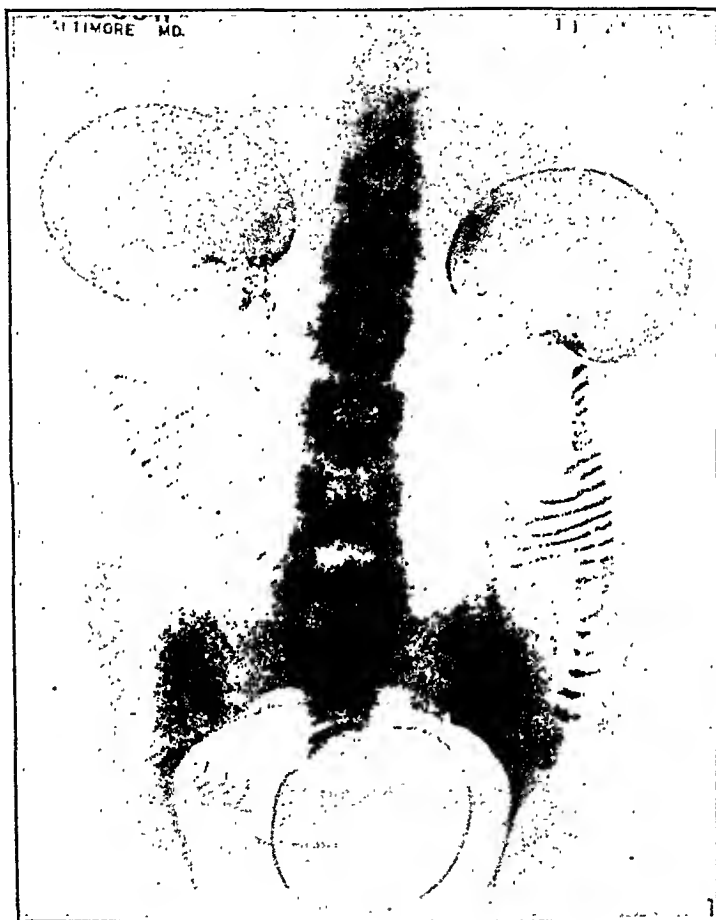


Fig. 1.

nor could more than one fetal heart sound be heard. A second x-ray taken two weeks after the first one revealed 2 fetal heads in the fundus and 1 in the pelvis (Fig. 1). The gain in weight continued, and on December 9, the patient weighed 129½ pounds. The height of the fundus was 30 cm., the distance from the symphysis to the top of the fundus around the ovoid was 38½ cm., and the circumference at the level of the umbilicus was 91 cm. During this time the patient felt well and had no complaints except some shortness of breath on exertion. The blood pressure remained around 120/80, urinalysis was negative, and hemoglobin was 80 per cent (Dare).

On December 10, at approximately thirty-one weeks of gestation, at 2:30 A.M., the foremost bag of waters ruptured spontaneously and labor pains began about one hour later. Labor progressed rapidly and normally. Pains were at three-minute

intervals, strong and lasting forty to fifty seconds. At 6 A.M. the cervix was completely dilated and the occiput of the first baby was on the perineum. Under gas-oxygen-ether anesthesia a left mediolateral episiotomy was done and low forceps applied. A 2 pound 13¼ ounce living female child was delivered at 6:05 A.M., position R.O.A. The second bag of waters presented and was ruptured artificially. This child presented as a footling breech with the back to the right. At 6:09 A.M. a 2 pound 13½ ounce living female child was extracted. After the delivery of the second child, the third one which had been a breech presentation with the back to the left turned spontaneously and presented by the occiput with the back to the right. The third set of membranes were ruptured and a combined podalic version followed by breech extraction was done. This child, also a female, was delivered at 6:17 A.M. and weighed 2 pounds 11½ ounces. The episiotomy was repaired with No. 2 chromic catgut, and the placenta and membranes were expressed intact by modified Credé method. There was very little blood loss but the patient's pulse rose to 120 per minute immediately following delivery and remained at that level for about half an hour, after which time it fell slowly to 80 per minute and remained at that level. The rise was attributed to the sudden decrease in intraabdominal pressure. The amount of amniotic fluid contained in each of the 2 sacs artificially ruptured was estimated at 1,000 to 1,500 c.c. The mother left the delivery room in

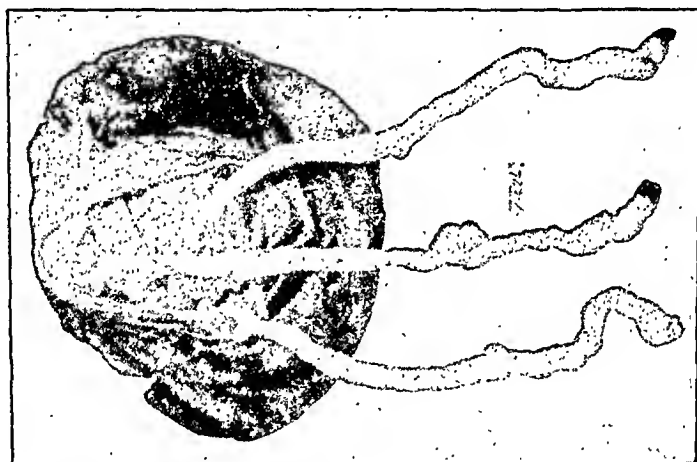


Fig. 2.

good condition. The puerperium was normal except for a rise in temperature to 100.8° F. on the fourth day and 101° on the fifth day, the pulse rate being 102 and 90, respectively.

All of the babies were normal but were very cyanotic and required resuscitation. After an hour in warm tubs and the administration of oxygen carbon dioxide they were breathing regularly, and their color was good although they cried poorly. They were then placed in premature cribs and taken to the premature room. Attacks of cyanosis recurred during the next few hours and six hours after delivery baby No. 2 died. A few minutes later baby No. 3 died during a cyanotic attack. Baby No. 1 died at the end of twelve hours in the same manner. The cause of death in all 3 was attributed to congenital atelectasis due to prematurity.

The placenta (Fig. 2) was large, round, and measured 18½ by 18 by 5 cm. The surface area was about that of the average placenta but the thickness was twice as great. It weighed 990 gm. or 490 gm. more than the weight of the normal placenta as given by DeLee.¹⁰ Both the maternal and fetal surfaces were normal in color, and there was no evidence of any gross pathology. There were 3 amniotic sacs but only one chorion. All of the amniotic sacs seemed to be approximately the same size and were easily demonstrated as the ruptures were small and some

distance from the placenta. The membranes were entirely normal. The cords were large and all about the same length, 29, 30, and 31 cm. One cord had a velamentous insertion and 2 had central insertions. The placenta indicates that the case is one of uniovular triplets.

I wish to express my appreciation to Dr. Louis H. Douglass for his assistance in the handling of this case and in the preparation of this paper.

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104 WEST MADISON STREET

EARLY CHORIONEPITHELIOMA ARISING IN HYDATIDIFORM MOLE*

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THE diagnosis of chorionepithelioma is facilitated by the Friedman test due to the fact that the concentration of anterior pituitary hormone in the patient's urine is much higher than in the urine of a normal pregnancy. One-seventieth of a cubic centimeter of urine from a patient afflicted with chorionepithelioma may be sufficient to evoke a positive reaction in mice.¹ However, after the expulsion of a hydatidiform mole and curettage of the uterus, there may be a long latent period before the development of the chorionepithelioma, as in the case of Kroesing, which had a latent period of five and one-half years.² In the absence of clinical signs, such as bleeding, cystic degeneration of the ovaries, or irregular enlargement of the uterus, it is difficult to know whether a malignant tumor will eventually develop in a uterus from which a hydatidiform mole has been removed. In the case reported herewith a repeatedly positive Friedman test was the only indication of persistent intact mole tissue or early chorionepithelioma of the uterus.

L. K., white, aged thirty-one, para ii, was admitted to the hospital on April 24, 1934, with a history of profuse vaginal bleeding of twenty-four hours' duration with passing of blood clots. This had been preceded by irregular spotting since March 18. Her last regular menstrual period occurred Feb. 17, 1934. Upon a pelvic examination April 1, the diagnosis of a two months' pregnancy with threatened abortion was made. The patient stated at that time that in her previous pregnancies she also spotted during her second month.

Her past history was essentially negative. Her husband was living and well. She had had full-term deliveries six and four years previously. Her first pregnancy was complicated by a severe pyelitis and the delivery by a postpartum hemorrhage

*Read at a meeting of the Obstetrical and Gynecological Section of the Cleveland Academy of Medicine, June 6, 1936.

necessitating transfusion. Her second pregnancy was normal, but the delivery was followed again by severe postpartum hemorrhage. No transfusion was done. The child was stillborn (congenital heart disease). Her menses had always been regular, of average duration and flow. Physical examination, serology, and urinalysis were negative.

On admission to the hospital a diagnosis of incomplete abortion was made. No vaginal examination was done. Routine treatment with pituitary extract did not empty the uterus and did not check the bleeding.

Dilatation of the cervix and curettage was then performed on April 25, 1934. The uterus was found to be the size of that of a three months' pregnancy, its depth being 5 inches. A large mass of tissue grossly characteristic of hydatidiform mole was removed, and the uterus was gently curetted and packed.

Microscopic Examination: Uterine contents: Section showed a striking picture; the tissue was composed of chorionic villi, the majority of which showed moderate to marked edema of the stroma. Some of the villi were over $1\frac{1}{2}$ mm. thick. The syncytium was thicker than average, nuclei of cells large. Final Diagnosis: hydatidiform mole (Fig. 1).



Fig. 1.

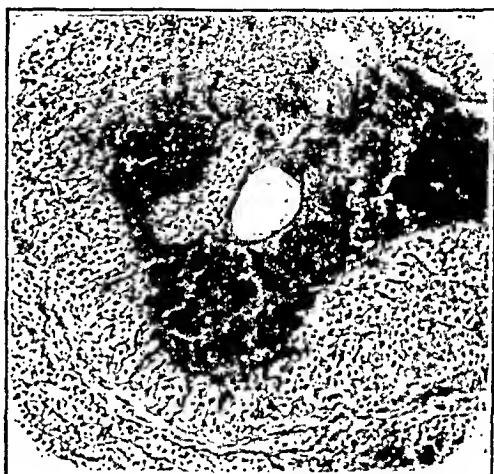


Fig. 2.

First. 1.—Photomicrograph, low magnification. Hydatidiform mole removed at first curettage.

Fig. 2.—Photomicrograph, low magnification. Rabbit ovary. Corpus luteum with hemorrhage and retained ovum (positive Friedman test).

The patient left the hospital in four days, at which time there was only a scant brownish vaginal discharge.

The admission specimen of urine (Apr. 24, 1934) gave a strongly positive Friedman test (Fig. 2), using $\frac{1}{2}$ c.c. of urine (Table I).

A second Friedman test performed May 16, 1934, about three weeks after removal of the mole, gave a weakly positive result using 30 c.c. of urine. Because of the fact that gonadotropic hormone was still present in the urine, another Friedman test was done June 8, 1934, and again gave a weakly positive result with 30 c.c. of urine.

Because of the persistently positive Friedman reaction, it was thought advisable to repeat the curettement to remove whatever mole tissue might have been left in the uterus after the first curettement. The patient was readmitted on June 21, 1934. Examination on admission showed the uterus well involuted, not tender, no enlargement or tenderness of the adnexa. The history of a slight intermittent brownish discharge was the only finding pointing to a possible retention of hydatidiform mole in the uterus.

Dilatation and curettage was done on June 22, 1934. The uterus was found to be about 3 inches deep and was firm. The uterus was curetted carefully, but vigorously, with a sharp curet. Only a small amount of endometrial tissue was obtained.

Microscopic examination of the curettings showed a few small islands of uterine endometrium with glands few in number. There was some proliferation of fibroblasts and focal areas of round cell infiltration in the stroma. No villi or hydatidiform mole were present. Diagnosis: subacute endometritis (slight).

TABLE I

DATE	FRIEDMAN TEST		SURGICAL PATH. DIAGNOSIS
	RESULT	AMT. URINE	
4/24/34	Strongly positive	0.5 c.e.	Hydatidiform mole
5/16/34	Weakly positive	30.0 c.e.	
6/ 8/34	Weakly positive	30.0 c.e.	
6/22/34			Chronic endometritis
7/20/34	Strongly positive	30.0 c.e.	
7/30/34	Strongly positive	20.0 c.e.	
8/ 4/34	Strongly positive	30.0 c.e.	
	Negative	0.5 c.e.	
8/13/34			Few intact villi of hydatidiform mole
8/25/34	Weakly positive	30.0 c.e.	
9/14/34	Weakly positive	30.0 c.e.	
9/18/34	Positive	30.0 c.e.	
9/24/34			Intact syncytial masses of mole in uterus. Beginning chorionepithelioma (?)
9/26/34	Negative	30.0 c.e.	
Postop.			
10/ 6/34	Negative	30.0 c.e.	
Postop.			
10/31/34	Negative	30.0 c.e.	
Postop.			
10/10/35	Negative	30.0 c.e.	
Postop.			

The Friedman test was repeated one month after her discharge from the hospital (July 20, 1934) using 30 c.e. of urine, and a strongly positive reaction was obtained. Ten days later (July 30) her urine again gave a strongly positive Friedman test with 20 c.e. of urine. This was rechecked August 4, and the result was as follows: Friedman test strongly positive with 30 c.e. and negative with $\frac{1}{2}$ c.e. of the patient's urine.

The patient was readmitted to the hospital August 12 solely because Friedman tests were persistently positive. The history and physical findings on this admission were entirely negative. There had been no vaginal bleeding or discharge since the last curettage seven weeks previously.

Curettage was again performed on August 13. The uterus was found to be about 3 inches deep and firm; no masses or irregularities were discovered on palpation. At one point in the curettage of the posterior wall profuse bleeding occurred. A small amount of endometrium was removed. The largest mass was about 6 mm. in diameter and appeared membranous, spongy and edematous. Microscopic examination of the curettings showed about a dozen typical chorionic villi of hydatidiform mole. The edema of the stroma was variable. In places some of the villi were over 1 mm. in width. The syncytium varied in thickness; in places it was heaped up with some of the nuclei, large and hyperchromatic. There was one small nest of cells several hundred micra in diameter, possibly decidua cells. Final Diagnosis: intact chorionic villi of hydatidiform mole.

Following this curettement a Friedman test was done Aug. 25, 1934, and was weakly positive with 30 c.c. of urine. On repeating the test about three weeks later, September 14, a similar reaction was obtained. However, a few days later, September 18, on repeating the test a somewhat more strongly positive result was obtained.

A pelvic examination on September 20 showed cystic enlargement of both ovaries to about three times the normal size. This finding, together with the fact that at no time was a negative Friedman test obtained with 30 c.c. of the patient's urine during the six-month period of observation, indicated increased hormonal activity resulting from the presence of living chorionic tissue in the uterus, and hysterectomy was decided upon.

The patient was readmitted to the hospital for the fourth time on September 23. She had no complaint. There was no vaginal discharge. The uterus was normal size, freely movable, not tender. The left ovary was cystic and four times the normal size. The right ovary was cystic and twice the normal size.

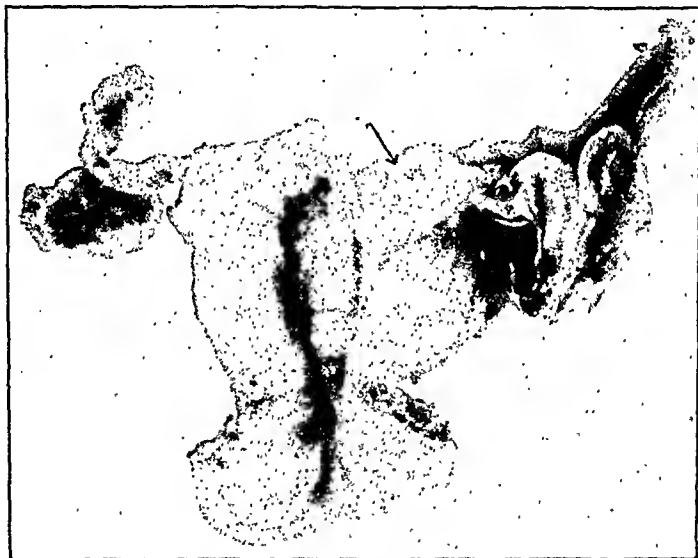


Fig. 3.—Gross photograph, actual size. Ovaries, fallopian tubes, uterus and cervix, showing necrotic mole mass in fundus and multiple cystic corpora lutea in ovaries.

On September 24 the following operations were performed: total hysterectomy, bilateral salpingectomy, left oophorectomy, and partial resection of the right ovary.

Laboratory Report: The uterus was of approximately average size (weighing together with the cervix about 65 gm.) and showed no appreciable abnormalities on the external surface. On opening the uterus the endometrial canal was not enlarged and the endometrium was thinner than average with no evidence of retained hydatidiform mole. On section of the myometrium, however, a striking picture presented in the upper portion of the fundus. Here a roughly spherical mass, about 12 mm. in diameter, was found reaching from just beyond the endometrium to within 1 mm. of the perimetrium (Fig. 3). The tissue here was friable in consistence and grayish yellow, grossly suggesting malignant tumor invading the myometrium. Microscopic examination of this area showed the tissue to be degenerating and necrotic tissue of hydatidiform mole (Figs. 4 and 5) and apparently not the tissue responsible for the positive Friedman tests. Further examination of the uterus to determine the cause of the most recent positive Friedman tests showed in the myometrium bilaterally toward the cornua small coherent masses of

grayish tissue in the walls of dilated and tortuous veins (Figs. 6, 7, 8, and 9). Sections from these areas showed very large syncytial cells or cell masses, some over 100 micra in diameter, adjoining one another in one or several layers immediately below the intima. The nuclei were very large, many hyperchromatic. In a few places coherent nests of these large cells were observed; the largest, about $1\frac{1}{2}$ by $\frac{3}{4}$ mm., suggested beginning or early chorionepithelioma formation. The majority of the cells here were apparently intact.



Fig. 4.



Fig. 5.

Fig. 4.—Photomicrograph, very low magnification (about $\times 6$). Degenerating and necrotic tissue of hydatidiform mole in myometrium of fundus.

Fig. 5.—Photomicrograph, low magnification. Degenerating and necrotic tissue of hydatidiform mole from area shown in Fig. 4.



Fig. 6.—Photomicrograph, very low magnification. Intact syncytial cells and cell masses lining veins in myometrium in cornua of uterus.

The fallopian tubes grossly appeared normal, but in the proximal end of the left tube there was a mass of friable whitish tissue in the wall several millimeters in diameter. Sections in this area showed, in the wall several hundred micra from the lumen, a mass 2 to 3 mm. in diameter, composed of necrotic mole tissue (Fig. 10).

The left ovary and the removed portion of the right ovary were both found to be enlarged by characteristic cystic corpora lutea (Fig. 3). There were two of these in the left and one in the right ovary, each measuring about 3 cm. in diameter. Microscopically, regional to a lutein cyst there was an island of typical decidual

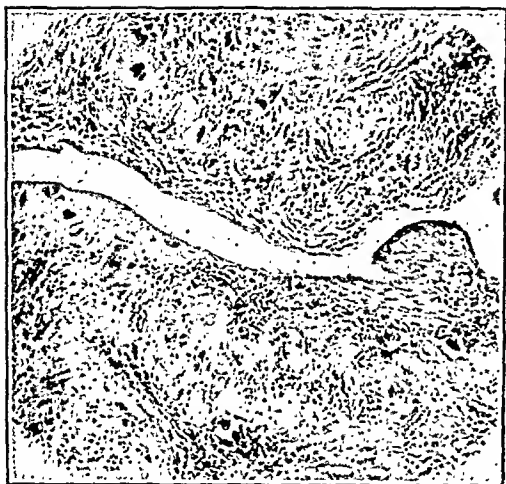


Fig. 7.



Fig. 8.

Figs. 7 and 8.—Photomicrographs, low magnification. Intact and degenerating syncytial cells lining veins in myometrium in cornua of uterus.



Fig. 9.



Fig. 10.

Fig. 9.—Photomicrograph, low magnification. Intact syncytial cells and cell masses with very large hyperchromatic nuclei lining veins, suggesting early chorionepithelioma formation.

Fig. 10.—Photomicrograph, very low magnification. Proximal portion of fallopian tube showing necrotic mole tissue in the wall.

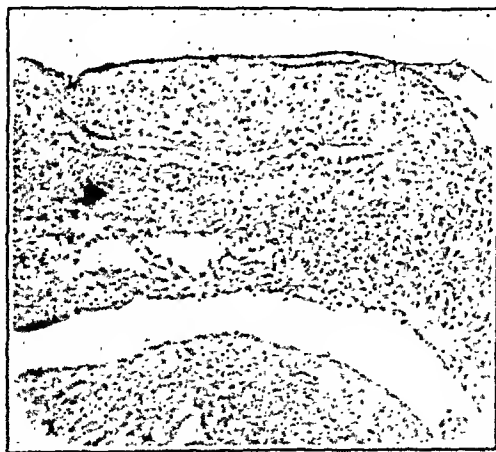


Fig. 11.—Photomicrograph, low magnification. Decidual reaction on surface of ovary (same magnification as Figs. 7 and 8) for comparison of size of nuclei of decidua cells and those of syncytium.

tissue several hundred micra in diameter just below the surface of the ovary (Fig. 11). There were also other smaller islands of similar decidual tissue at some distance just below the surface of the ovary.

Final Diagnosis: Multiple islands of intact syncytial cells in the walls of veins in the myometrium especially in the region of the left cornua. One island $1\frac{1}{2}$ mm. diameter (beginning or early chorionepithelioma?). Disseminated intact hydatid mole masses in veins of uterus especially at left cornua and right lateral portion of fundus. Multiple areas of degenerating syncytial cells with replacement fibrosis in the walls of veins. Extension of hydatidiform mole into myometrium of fundus in an area $1\frac{1}{2}$ cm. diameter reaching to within 1 mm. of the perimetrium (degenerated). One mole mass in wall of proximal portion, left fallopian tube (degenerated). Multiple cystic corpora lutea, ovaries largest about 3 cm. diameter.

The Friedman test on Sept. 26, 1934 (forty-eight hours after operation) was negative. The patient made a most uneventful recovery and left the hospital twelve days after operation. The Friedman test on the day of discharge was negative. It was also negative Oct. 31, 1934, and Oct. 10, 1935. At the time of the present report (Nov. 1, 1935), the patient has no complaint and the pelvic findings are entirely negative.

COMMENT

The incidence of chorionepithelioma following hydatidiform mole has not been definitely established. Findlay reports a series of 500 cases of hydatid mole. In 157 of these, chorionepithelioma developed, an incidence of 31.4 per cent.³ In Senarden's series of 49 moles, 5 or 13 per cent developed chorionepithelioma; while Williams states that in his experience only 5 per cent of hydatidiform moles underwent chorionepithelioma⁴ formation.

Because of such variation in the incidence of chorionepithelioma developing in hydatidiform moles recorded by different observers, the method of treatment is often debatable. One of the authors (M. G.) has sent the complete history of this case to twelve outstanding obstetricians and gynecologists of his city asking their opinion as to what treatment was indicated. Fifty per cent of the responses were in favor of immediate hysterectomy, while the rest advised watchful waiting.

During the six months that elapsed from the discovery of the mole to the hysterectomy, the Friedman test remained positive with 30 e.c. of the patient's urine, and repeated pelvic findings were negative. As soon as the Friedman test appeared more positive and the ovaries showed a cystic enlargement, the operation was performed without delay.

It appears, then, that repeated examination of the patient's pelvis, together with repeated Friedman tests, may be used as a reliable guide in solving the often perplexing problems of the treatment of hydatidiform mole.

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The author reports a case of pruritus vulvae cured by phenolization of the pelvic sympathetic nerve after having resisted all other known treatments for fifteen years.

AUGUST F. DARG.

STUDIES ON BARBITURATES. XIV

THE PLACENTAL TRANSMISSION OF NONANESTHETIC DOSES OF BARBITAL

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ANESTHETIC doses of barbital and amytal have been shown to pass from the blood of the mother into the fetus.¹ In these experiments single anesthetic doses of sodium barbital (from 225 to 300 mg. per kg.), and amytal (100 mg. per kg.) were administered intravenously to pregnant rabbits, and the amounts of barbiturate present in the fetus, amniotic fluid, and placenta were determined by colorimetric methods for the quantitative estimation of barbiturates developed by Koppanyi et al.^{2,3} It was found that appreciable quantities of these two barbiturates were present in the fetus fifteen minutes after the administration of the drug to the mother, and in some cases the quantity approached a concentration which could be deemed anesthetic. However, in all cases the fetuses were viable as shown by their response to mechanical stimuli. Since the doses used in this work were higher than those used in human obstetrics, the possibility arises that in smaller doses barbiturates are not transmitted through the placenta in detectable amounts. The following experiments were devised to investigate this possibility.

EXPERIMENTAL

Sodium barbital (soluble barbital, "medinal") in doses of 75 and 100 mg. per kg. was administered to rabbits by the marginal ear vein. These amounts are sedative and soporific for rabbits, but never produce true anesthesia. This drug was chosen for this work in preference to other barbiturates, because a fairly large amount of it may be given without obtaining profound depression of the central nervous system, and thus it is easier to estimate accurately the amounts of drug present in the tissues without administering anesthetic doses.

In previous experiments when barbiturates were used in anesthetic doses, the surgical procedures involved could be easily carried out. In this series of experiments, however, since nonanesthetic doses were administered, the surgical procedures could not be performed without further anesthesia. Therefore, for immobilization and analgesia of the experimental animal, spinal anesthesia was used in every case. One cubic centimeter of a "light" type of spinal anesthetic (novocaine 0.195 gm., starch 0.130 gm., alcohol 0.324 c.c., and physiologic saline q.s. ad 2.000 c.c.) was injected into the third lumbar interspace and after the maximum effect was obtained the rabbit was placed on an animal board, head downward, and the requisite dose of sodium barbital injected. After laparotomy and exposure of the uterus two or more fetuses were removed at various intervals by clamping off and excising the portion of the uterus containing the fetus. Care was taken not to interfere with the circulation of the remaining portion of the uterus, which was returned

to the abdominal cavity and the wound temporarily closed until the removal of the next uterine portion. The excised portion of the uterus was opened longitudinally, and the amniotic fluid was collected without contamination with blood by aspirating it from the amniotic sac with a syringe. The fetus was separated from the placenta and fetal membranes, and tested for viability by pinching a fold of the skin with forceps.

The fetuses, the placentas, and amniotic fluids were prepared for barbital determinations separately. The fetuses were weighed, hashed in a meat grinder and the proteins precipitated and removed by filtration according to the alkaline-copper sulphate method described by Koppanyi et al.^{2,3} The placentas were treated likewise. The amniotic fluid was measured and treated with equal amounts of 10 per cent sodium tungstate and 5 per cent sulphuric acid, shaken vigorously to precipitate the proteins and filtered. The protein-free filtrates were then extracted with chloroform. All chloroform extracts of the filtrates were concentrated by evaporation and tested by the microtest of Koppanyi et al.³

TABLE I. THE CONCENTRATION OF BARBITAL IN THE AMNIOTIC FLUID, PLACENTA AND FETUS FOLLOWING INTRAVENOUS ADMINISTRATION OF SODIUM BARBITAL TO THE MOTHER

RABBIT	DOSE MG./KG.	TIME ELAPSED BETWEEN IN- JECTION AND REMOVAL OF THE FETUS	AMNIOTIC FLUID MG./C.C.	PLACENTA MG./GM.	FETUS MG./GM.
1	75	1 min.	trace	trace	trace
		15 min.	0.040	0.015	0.008
		30 min.	0.025	0.023	0.010
		60 min.	0.025	0.024	0.010
2	100	1 min.	----	0.029	0.017
		15 min.	----	0.023	0.014
		30 min.	0.013	0.015	0.027
		60 min.	----	0.048	0.048
3	100	5 min.	0.010	0.010	0.008
		30 min.	0.017	0.025	0.022

Table I contains a summary of the results obtained using doses of 75 and 100 mg. of sodium barbital per kilogram. With these doses, as with the larger doses used in previous work, a transfer of barbital from the mother to the fetus could easily be demonstrated. Barbital was found in the placenta and in the amniotic fluid as well as in the fetus. The amount of barbital accumulation in the placenta and fetus increased steadily within the first hour following intravenous injection. To approximate conditions existing in normal obstetric use, only pregnant rabbits which were near the end of gestation, when the weight of the fetuses was about 15 to 20 gm., were selected for these experiments.

COMMENT

The doses of barbital administered to these pregnant rabbits represent less than one-half of the minimum amount of this drug required to produce surgical anesthesia. Corresponding doses of other barbiturates are frequently employed in obstetrics to produce amnesia and analgesia, and from these experiments, it is evident that doses of this magnitude permeate the placenta just as easily as anesthetic doses. In our previous work it was shown that the placenta presents no barrier against full anesthetic doses of barbituric acid derivatives,

and this is also true for doses producing only light depression. There is little doubt that what holds true for these smaller doses of barbital also applies to corresponding doses of other barbiturates. At any rate, no one can now maintain that the placental permeability to barbiturates exists only after large doses have been administered.

In the experiments described above, all of the fetuses removed from the uterus showed respiratory movements and reacted to mechanical stimuli. They were not anesthetized, in fact they could not be, for no anesthetic doses had been administered to the mother. But the fact that fetal tissues contained appreciable amounts of barbiturates is a fairly certain indication that some degree of central nervous depression must have been present in the fetuses, and that the degree of this narcosis of the fetus will depend upon the size of the dose administered to the mother. While we are not prepared to state that pregnancy offers a contraindication to the use of barbiturates, we must call attention to the fact that the placenta offers no barrier to barbiturates, and that whenever these drugs are administered to expectant mothers, the embryo will get its full share of them.

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ERGOT IN THE PUERPERIUM

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THE clinical value of ergot in the puerperium has long been questioned by various obstetricians. However, Koff¹ and Moir² have definitely proved that ergot has a marked oxytocic effect and an important place in the puerperal management of a modern obstetric case. In view of the divergent opinions on the importance of ergot, we have studied the morbidity, involution, and puerperal bleeding in 551 post-partum cases on three different ergot regimes in the Kensington Hospital for Women.

PROCEDURE

In each case every patient received an ampule of pituitary solution and ergot at the completion of the second stage of labor. The first 100 patients received no other oxytocic medication during their stay in the hospital. A series of 351 patients received fluid extract of ergot, U.S.P., starting when the patient was taken to her ward bed. Here she received one drachm every four hours for six doses, and then three times a day for four days. In the third group of the series, 100 cases, an ergot preparation* was used which was standardized for its content of the new

*Ergoklenin, supplied through the courtesy of John Wyeth and Brother, Inc.

alkaloid, ergostetrine³ (ergometrine). This was administered in the same way as the fluid extract. In those cases where lochia rubra was present to any great extent after the sixth postpartum day an additional course of one drachm at four-hour intervals for six doses was administered. Thirty-five per cent of the patients on fluid extract of ergot, U.S.P., needed this and 20 per cent on ergoklonin received additional dosage. Upon discharge date, the morning of the tenth day, a sterile vaginal examination was done on all patients that did not have repair work following delivery. At this time note was made of the involution of the uterus, the amount of bleeding, and the gross uncorrected morbidity.

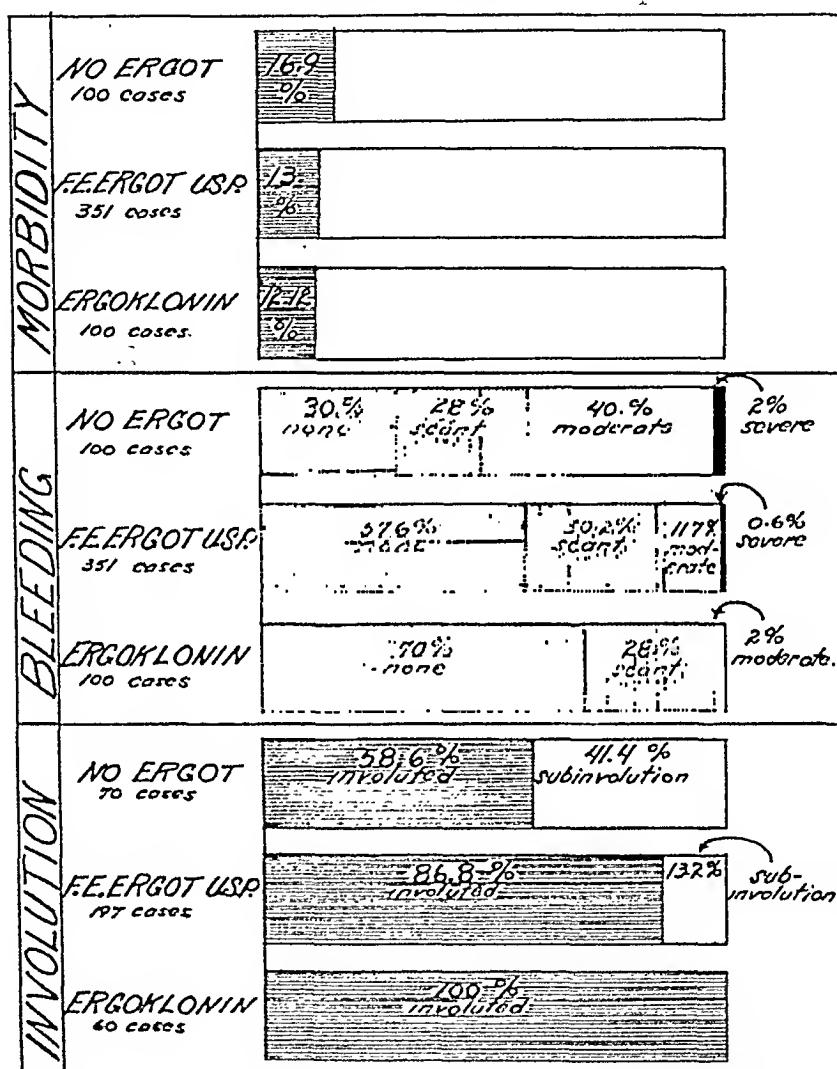


Fig. 1.—Comparison of involution, degree of bleeding and morbidity in patients on different regimes during the puerperium.

RESULTS

Involution.—In patients not receiving ergot, subinvolution occurred in 41.4 per cent of the patients examined (Fig. 1) and in 13.2 per cent of the patients of the fluid extract series, while no subinvolution occurred in the patients receiving the newer ergot preparation.

Bleeding.—A striking difference in the lochia rubra was noted on the tenth day (Fig. 1). The best result was obtained with ergoklonin, since 70 per cent of that group had no sanguineous discharge. The fluid ex-

tract series showed bleeding to some extent in all but 57.6 per cent, while in the cases without oral ergot only 30 per cent were entirely free of bleeding. In the patients classified as showing scant bleeding (Table I), there was a low incidence of subinvolution, and these may therefore be

TABLE I

DEGREE OF BLEEDING	NO ERGOT				F. E. ERGOT U.S.P.				ERGOKLONIN			
	100 CASES				351 CASES				100 CASES			
	PER CENT	INVOLUTED	SUBINVOLUTION	NO EXAMINATION	PER CENT	INVOLUTED	SUBINVOLUTION	NO EXAMINATION	PER CENT	INVOLUTED	SUBINVOLUTION	NO EXAMINATION
None	30	21	2	7	57.6	117	3	82	70	40	0	30
Scant*	28	16	4	8	30.2	44	11	51	28	18	0	10
Moderate	40	4	22	14	11.7	10	11	20	2	2	0	0
Severe	2	0	1	1	0.6	0	1	1	0	0	0	0

*Scant bleeding: a few drops of fresh blood or a mucosanguineous discharge.

Moderate bleeding: a saturated vulval pad in six hours.

Severe bleeding: several saturated pads in six hours.

grouped with the nonbleeding series from the standpoint of a satisfactory puerperium. The groups showing moderate bleeding demonstrate clearly the value of oxytocic medication during the puerperium, for 40 per cent of the nonergot cases fall in this classification, while only 11.7 per cent in the fluid extract series, and 2 per cent in the ergoklonin series showed hemorrhage of this magnitude. The "severe bleeding" classification is represented by 2 per cent in the nonergot group and 0.6 per cent in the fluid extract cases. No cases of this type occurred in the ergoklonin group.

Morbidity.—A patient was considered as morbid when her temperature reached 100° F. twice in twenty-four hours, excluding the first postpartum day. These figures are uncorrected and constitute all temperatures, no matter what cause, that appeared in these 551 cases. The morbidity was highest (16.9 per cent) (Fig. 1) in the patients who received no ergot and lowest (12.12 per cent) where ergoklonin was used, while the fluid extract of ergot, U.S.P. series differed only slightly from the new preparation, at 13 per cent.

CONCLUSIONS

1. Lochia rubra was more persistent in patients receiving no form of ergot during the puerperium.

2. Subinvolution occurred in much higher percentage (41.4 per cent) in nonergot cases than in fluid extract cases (13.2 per cent), and was completely absent in the ergoklonin series.

3. A satisfactory puerperium was observed in 58 per cent of patients receiving no oxytocic drug, in 87.8 per cent of patients receiving fluid

extract of ergot, U.S.P., and in 98 per cent of patients treated with ergoklonin. There was less striking difference in the morbidity percentages in the three groups than in the figures showing degree of bleeding and subinvolution.

4. From a study of a series of 551 cases, ergot appears to be a useful and necessary aid to a normal puerperium, preferably in the form of a preparation of known ergostetrine (ergometrine) content.

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RECOGNITION AND PREVENTION OF BLADDER INJURIES

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ON FIRST thought, a discussion of the subject indicated in the title of this paper would appear superfluous and exceedingly elementary. However, when one reads the literature and finds that the mortality in bladder injuries during operation is variously reported as from 12 to 45 per cent, it is apparent that the subject, after all, does deserve attention, especially as most cases remain unreported.

My own attention was drawn to this subject by a few observed and below described personal cases. My experience leads me to conclude that this injury is not a serious complication, provided that it is recognized and promptly and properly treated. Once the accident is recognized, surgical victory is almost surely attained, for treatment is simple and practically always successful.

This subject is of particular interest to the pelvic surgeon who of necessity employs the suprapubic incision in the great majority of cases, and as a corollary the bladder is in much greater danger than in other types of surgery except that of hernia. It is especially in jeopardy in cases of large fibroids of the uterus where the bladder is displaced and stretched and is likely to be found at a much higher level than normally. Practically all of my observed and personal cases of bladder injury occurred in large fibroids of the uterus.

CASE 1.—Mrs. L. M., forty-seven years old, gravida vii, para iii. Chief complaints: enlargement of the abdomen, dribbling of urine, and profuse menstrual flow.

Abdominal examination showed a mass in the center of the abdomen, hard, not tender, reaching from the symphysis to the umbilicus. Vaginal examination disclosed a marked cystocele, lacerated cervix, uterus the seat of tumors reaching to the umbilicus.

At operation, there was found a degenerated cystic mass which was firmly adherent to the parietal peritoneum and intestines and attached to the fundus of the uterus by a short pedicle. The tubes and ovaries appeared normal. The liver

was smooth and the gallbladder was normal. A median suprapubic incision was made, and a large amount of serous fluid escaped from the peritoneal cavity. The tumor was separated from the intestines and parietal peritoneum. One of the cystic masses opened during manipulation. The pedicle of the tumor was clamped, and the tumor was removed. A supravaginal hysterectomy was then performed, all raw surfaces were peritonized, and the abdomen was closed in layers, without drainage.

A culture from the intraabdominal fluid found free in the peritoneal cavity was found sterile.

The uterus contained many small intramural fibroids and measured 6 by 6 inches. The wall was very thick and the mucosa hypertrophic. The intramural fibroids appeared somewhat degenerated. Another mass distinct from the uterus was globular in shape and measured 9 by 8 inches. It included two large multilocular cysts with serous, yellow, gelatinous contents. The cyst wall was very thin, smooth and did not contain any papillae. The solid portion of the mass was yellowish in color, fatty and was also somewhat cystic.

Diagnosis: Cellular myomas of the uterus, pedunculated myoma with cystic degeneration, and marked endometrial hyperplasia.

Sections from various portions of the uterus and from the pedunculated mass showed extremely cellular leiomyomatous tumors which did not appear aggressive enough to warrant diagnosis of malignant transformation.

Postoperative Course: Patient was comfortable the day of the operation. She was catheterized twelve hours afterward and no urine was obtained. An intravenous infusion of glucose and saline was given, and she was again catheterized and only a few drops obtained. The nurse reported that the patient was almost continuously dribbling. A later catheterization yielded 25 c.c. of urine. The bladder was filled with argyrol solution and practically the same amount was obtained by catheterization as was introduced. The chemical examination of the blood showed a nonprotein nitrogen of 35, and a CO_2 of 40. Hot fomentations were applied to the kidney regions and hypodermoclysis and intravenous infusions were continued. A urologist was called in consultation, and he was of the opinion that the ureters were not tied, that there was no injury to the urinary organs, and that the patient was suffering from reflex anuria. The patient died about seventy-two hours after the operation.

Autopsy Report: On opening the abdominal cavity the viscera were found covered by plastic exudate and slightly adherent to each other. Line of suture was intact. On inserting a probe into the bladder there was found a small collapsed opening in the roof of bladder which connected with the peritoneal cavity. The opening was found to be the only part of a large surgically produced defect in the roof of the bladder, most of which was closed by inclusion within the sutures closing the peritoneal cavity. It was impossible to discern within the peritoneal cavity any argyrol which had been introduced into the bladder or any indigo carmine which had been injected intravenously. The bladder was empty and the mucosa congested. The microscopic examination of the kidneys and pelvic lymph nodes showed them to be normal.

CASE 2.—Mrs. R. F., aged twenty-five years. In the course of an examination for a gastrointestinal upset, her family doctor discovered a large tumor of the uterus. In retrospect, the patient recalled being troubled with urinary frequency. An abdominal examination revealed a large ovoid mass reaching from the symphysis to the umbilicus.

Operation: Median suprapubic incision, the bladder was very high and attached to the uterus. The bladder was dissected off and in doing so a small piece of adherent bladder was opened into. The rent was immediately repaired by two layers of sutures. A cigaret drain was placed in the pelvic cavity behind the cervical stump, and a piece of Penrose tubing was placed over the cut area. A retention catheter was placed in the bladder.

The uterus measured 10 by 6 inches, and contained several hard fibroids. The patient made an uneventful recovery.

CASE 3.—Mrs. F. H., aged forty years. Chief complaints: lower abdominal pain, enlargement of the abdomen, and menorrhagia. Vaginal examination revealed the presence of a uterus reaching from the pelvic basin to the level of the umbilicus. Multiple tumors were palpable. The patient was catheterized on the operating table and the catheter was left in situ. A suprapubic incision was then made and a typical supravaginal hysterectomy was performed. The bladder was at a much higher level than normally and was cut into. No urine escaped but the fact that the structure was bladder, was confirmed by feeling the catheter. The bladder injury was treated exactly as in the case cited above. The patient made an uneventful recovery.

CASE 4.—Mrs. L. B., aged forty-two years. The signs and symptoms were similar to those in Case 3. This patient was also catheterized on the operating table, and the catheter was left in situ. A suprapubic incision was made and a supravaginal hysterectomy was performed. A small intraligamentous fibroid was also removed. Toward the latter part of the operation, the bladder was opened. Recognition of this accident would have been doubtful had it not been for the presence of the catheter in the bladder. The bladder rent was repaired as in the two cases cited above, and the patient made an uneventful recovery.

In order to avoid this, to say the least, embarrassing complication, I have lately been employing the following method to identify the bladder: The patient is catheterized and the bladder urine is allowed to escape. The catheter is left in situ, and by means of a glass connecting tip and rubber tubing the catheter is connected to a glass calibrated reservoir suspended from a movable column stand. This tube rests on the patient's thighs and lies under sterile drapes. There is an additional connecting glass tip in the tubing between the reservoir and the catheter. The reservoir is the usual "clysis" or intravenous bottle. I usually have it filled with 300 c.c. of 4 per cent boric acid solution, and a nurse releases the clamp on the tubing and allows the bladder to fill as soon as, or just before, I commence the abdominal incision. As soon as I have recognized the bladder, I open into the peritoneal cavity, and the nurse then allows the bladder fluid to drain off by disconnecting the glass connecting tube which lies outside the sterile drapes. Should it become necessary to refill the bladder, it is a very simple matter to again reconnect the connecting glass. The catheter is removed after completion of the operation.

Since I have been filling the bladder, I operate with much greater comfort. I feel that I am treading on much surer ground. The chances for inadvertently opening the bladder are very greatly diminished, and should this accident occur, it would be very easily recognized and repaired.

Leaving a catheter in situ, even without distending it, is a valuable aid in recognizing the bladder.

I am convinced that bladders are at times opened, and if the bladder is empty, the fact that the bladder has been opened frequently escapes recognition. Peritonitis results, and if autopsy is not performed, the cause of the peritonitis is ascribed to some other factor.

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1882 GRAND CONCOURSE

ENDOMETRIOSIS OF THE UMBILICUS

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UNDER the caption of heterotopic endometrial growths are included such structures or tissues which morphologically and in certain respects functionally resemble the uterine mucosa, although not necessarily coming in direct contact with the latter.

The theoretic origin of and the bizarre nomenclature ascribed to the specific neoplasm under discussion has been fully dealt with elsewhere. cursory reference to the theoretical phases should therefore suffice when emphasizing more important points in the cases here reported.

Lauehe,¹ assuming that under proper conditions coelomic cells are capable of transmutation into endometrium, probably has the advantage over advocates of other theories, because his reasoning rests firmly upon an embryologic foundation which is all inclusive, in that the wolffian body and müllerian ducts which are brought in for culpability as etiologic factors are developmentally of coelomic origin (Cullen²).

CASE REPORTS

CASE 1.—(Record No. 38359.) Mrs. M. C., aged forty-three years, white. Previously admitted November, 1926, and operated upon by Dr. George Gray Ward, including curettage, trachelorrhaphy, perineorrhaphy, rectopexy, myomectomy, oophorectomy, fixation of prolapsed ovary. The pathologic diagnosis was glandular hyperplasia of the endometrium, cervicitis, hemorrhagic ovarian cyst, normal appendix, myomata uteri. Patient was relieved of symptoms, and the wound healed by primary union. She was discharged on Nov. 24, 1926. Patient readmitted April 22, 1930. There was a lump in the umbilicus, which was first noticed in June, 1928. On examination a nodule which was tender, red, and hard, was found. On March 6, 1930, examination revealed an increase in size of the mass, which was now uncomfortable; it was inclined to bleed a little and was tender.

At the operation a neoplasm of the umbilicus, the size of a large acorn was observed; it was solid, tender, bluish in color, increasing in size, entirely free from surrounding tissue in the abdominal wall and free from any connection with the peritoneum. The mass was excised in its entirety when incising the abdominal wall.

Examination.—A firm node covered with stretched skin presenting a few purplish vesicular formations the size of a millet seed. A transection revealed the nodular

mass composed of whitish tissue septa which included in the meshes small cystic formations. Larger structures of the same type were filled with brownish, blackish thick fluid similar to old blood. The surrounding fat tissue was well delimited from the tumor, which did not seem to encroach upon it.

Serial sections of the whole mass were made, and every fifth and tenth section was prepared for microscopic studies. The epidermis covering the mass varied in thickness and appeared normal. The nodular projections were produced by the inclusion of groups of glands, which were in most instances a dense dissemination of lymphocytes. Glands were of different sizes; their shape and the type of epithelium corresponded to endometrium; a secretory function was apparent in some of them. Where cystic distention had occurred, the epithelium was flat or of cuboidal type. The fibroepithelial structures were densely scattered in the periphery of the mass, while in the central portions the epithelial structures were almost missing and diffusely arranged strands of cytogenic tissue only were encountered.

There was no borderline between the corium and the fibroepithelium inclusions which were also found below the fascia. In this area the epithelium was generally of nonsecretory, moderately atrophic type. One of the glandular ducts was dilated to a small cystic formation which was occupied by small lobules of fatty tissue. Near to it was a strand of loosely arranged cytogenic stroma in which polynuclear giant cells were densely distributed.

Since the peritoneum was not demonstrable in any of the sections, a continuity of the endometrial structures with the peritoneum could not be made evident. There were no specific epithelial formations found in the lower part of the sub-fascial layer and in the muscle. There was no evidence of inflammation.

Diagnosis.—Adenoma of umbilicus of endometrial type (endometrioma of umbilicus).

CASE 2.—(Record No. 59718.) Mrs. S. G., aged thirty-three years, colored. She was admitted June 10, 1935. Operator: Dr. A. J. Murphy. Patient complained of soreness and bulging of navel for four years. Her menses recorded $12 \times 28 \times 6-9$, occasional clotting, no dysmenorrhea, last regular period May 20. She had been married for thirteen years and was never pregnant. She was never operated upon. The umbilical swelling about the size of the "tip of finger" was getting progressively worse. She was not aware that coughing or exertion caused any increase in the size of the growth.

On operation a small umbilical hernia was found; there was no intestine or omentum in the hernial sac.

Clinical Diagnosis.—Umbilical hernia.

Gross Specimen.—Excised umbilicus with subcutaneous tissue. The umbilicus proper was converted into a dome-shaped elevation 2 cm. in diameter. The lower severed surface revealed a funnel-shaped indentation in which scar tissue was apparent. A transverse section through the specimen opened a cyst cavity which was partly filled with tarlike liquid. Its upper portion was composed of the projecting umbilicus. A smaller compartment laterally was lined with smooth serosa and released clear fluid. The tissue surrounding the cystic cavities was yellowish, firm connective tissue.

The endometrium presented a premenstrual phase. The myometrium was regularly built. Myomas changed from microscopic sizes to the large sizes described and revealed in all instances of typical structure. The serosa of the uterus was greatly thickened in areas and included minute cystic formations at such places, which were partly lined with flattened unspecific epithelium, in some instances of higher cuboidal type. There were multiple calcified deposits, many of them of the type of psammoma bodies. The section through the umbilicus revealed cystic cavities

lined with a folded, generally cuboidal epithelium arranged in a simple row. In one area short papillas were noted, the stroma of which included aggregated pseudoxanthoma cells. In a single spot a polypus structure was found built of the same structures as endometrium with a stroma infiltrated with round cells. Glands bore the characteristics of endometrial glands, however, did not show secretory function. Fragments of organized blood coagula were either adherent to the inner surface or lying free in the lumen. The subjacent stroma of the cyst wall which did not differ from the subcutaneous tissue was occupied in parts by hemorrhage of old age. Other cystic compartments described in gross examination bore the same epithelial lining, however, did not include structures identical with endometrium.

Diagnosis.—Adenofibrohyperplasia of umbilicus (endometriosis).

CASE 3.—(Record No. 60217.) Miss A. S., aged forty years, single, white, was admitted Aug. 28, 1935. Her chief complaint was bleeding from the umbilicus three to four days prior to each period for the last four or five years. Catamenia $13 \times 28 \times 2.5$ without pain or clots; last menses August 1, likewise regular. She was not married and never pregnant. No previous operation. Except for umbilical symptomatology and occasional parietal and occipital headaches just prior to her periods and a feeling of pelvic pressure or heaviness, and a rapid gain in weight during the last four years, patient otherwise felt and looked well.

At operation a granular cervicitis and inclusion cyst of the vagina were found. There was no growth on, nor enlargement of the umbilicus which was normal in contour. Probing with a very fine wire did not detect any opening through which bleeding from deep structures might have occurred. There was nothing to indicate any peritoneal attachment or abdominal continuity of the umbilical scar with any intraabdominal structures, as incision was advanced down to the peritoneal cavity.

Pathologic Examination.—Clinical diagnosis: endometriosis of the umbilicus. The gross specimen showed an umbilicus which was continuous with a concentric tumorlike enlargement of the subcutaneous fat tissue and measuring about 1 cm. in diameter. Microscopically the tumor of the umbilicus was composed of glands lined with cuboidal and cylindrical epithelium which was similar to that found in the derivatives of the müllerian duct. The glands formed adenoma-like structures, producing lobules separated from each other by a more or less broad layer of fibrous tissue. The individual glands were surrounded in some instances by thin layers of cytogenic stroma, resembling the endometrial. The glands were very close to the squamous epithelium covering the external surface. Some of the glands were cystically dilated and lined with flattened low cuboidal epithelium. The stroma around the glands included greatly engorged, large, thick-walled blood vessels and massive aggregations of pseudoxanthoma cells.

Diagnosis.—Partly cystic endometroid adenofibroma of umbilicus (endometriosis).

No complaints referable to original umbilical pathology in any of these cases recorded in follow-up to date. In none of the three patients was there any connection of the umbilical structures with any peritoneal or intraabdominal tissues. Similar findings have been reported by Green,³ Goddard,⁴ Zitronblatt,⁵ Keitler,⁶ Schiffmann and Seyfert,⁷ and Roques.⁸ It is relatively infrequent that such heterologous pathologic tissue has no connection with the peritoneum.

The total of reported cases throughout the world at the end of 1935 is sixty-eight.⁹⁻¹⁷

It is noteworthy, that a predominance occurs in white individuals. No case has been reported from Africa, the Far East, or the Orient, yet the colored individuals are not immune as indicated by our Case 2, Record 59,718 and the reports of others.

COMMENT

Absence of tumor (visible or palpatory) must be evidence of an exfoliative or desquamative process in the umbilical tissue when the bleeding occurs. Such an outcome may probably be the end-result of a conditioning influence exerted by an estrogenic hormone, which as is known appears in the blood in greater concentration during the premenopausal and early menopausal periods. The dormant endometrial structures becoming activated by a more pronounced stimulus, then begin to function, as was probably the effect in Case 3, where for twenty-two years of the patient's twenty-seven active menstrual years, no bleeding had occurred.

The result indicated must be predicated upon the presence of endometrial tissue in the umbilicus, derived most likely from an embryologic coelomic residuum or cell arrests, which, judging from the infrequency of such pathology (3 in 37,355) gynecologic cases reviewed in this study (the largest on record) occurs in an extremely circumscribed number of female ontogeny, in which the culpable cells, possessing potentiality for future differentiated biologic characteristics, begin to function for the first time under proper stimulation, probably hormonal (gonadotropic prolan A), or as the result of the removal of some anti-hormonal control.

The temptation to hypothesize in an endocrine sphere, in seeking a solution to some of the problems presenting themselves under the aforementioned caption, provokes the thought that at least some endocrine factor is responsible, particularly during the stage of gradual spontaneous castration (premenopause-menopause decade) due to a sort of reversed reciprocal relation between the ovaries and the gonad-stimulating cells of the anterior pituitary.²⁰

It may readily be that the same explanation holds true for younger women in whom, as a result of a genital crisis, hyperfunctional reaction of the hypophysis occurs similarly, bringing about the same activation.

Witherspoon²¹ has advanced a similar thesis and has attempted to prove by his pathologic material that the igniting factor of endometrioma has its origin in the excessive stimulation of the aberrant tissue, by the ovarian follicular hormone (prolan A). When this hormone's action is abnormal, there is produced a cellular metaplasia of the potential serosal cells or tumor proliferation of an aberrant endometrial implant, in short, the hormone is responsible for endometrial flowering.

Although operation offers a ready method for the relief of the symptoms associated with umbilical endometriosis, we must be mindful of other means at hand, to be used especially during the menopausal decade, in counteracting hormonal activation of endometrial tissue. Where the indications exist, the catalytic action of x-ray and radium may serve a well-defined purpose.

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304 WEST SEVENTY-FIFTH STREET

GRANULOSA CELL CARCINOMA

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THIS case is reported as an addition to the increasing list of granulosa cell carcinomas.

Mrs. A. M., fifty-two years of age, was admitted to the Jersey City Medical Center Nov. 24, 1931 with the diagnosis of metrorrhagia.

In May, 1931, the patient noticed uterine bleeding accompanied by backache. The bleeding was intermittently scanty or profuse without any definite cycle and persisted until admission to the hospital. The menstrual history was normal. She has one child living and well. Menopause occurred at the age of forty-seven.

Physical examination revealed nothing unusual, except an obese female with turgid and prominent breasts. The pelvis showed a hypertrophic cervix, rectocele, and a third degree prolapse of the uterus. The red blood count was 3,450,000, hemoglobin 65 per cent (Tallqvist), the white count 11,500 and the differential count, 81 per cent polymorphonuclears, 17 per cent lymphocytes, and 2 per cent large monocytes. All other clinical laboratory findings were negative.

Dec. 31, 1931, a total vaginal hysterectomy, perineorrhaphy and repair of the rectocele were done. Uneventful recovery followed the surgical intervention and the patient was discharged Jan. 23, 1932.

The pathologic report disclosed hypertrophy of the uterus with endometrial and cervical glandular hyperplasia. It is worth mentioning that the uterus measured 10 cm. from the fundus to the external os, 7 cm. in lateral diameter and 5.5 cm. in anteroposterior diameter.

Readmission: In January, 1933, the patient noticed a mass in her lower abdomen. On April 16, 1933, because of the progressive enlargement and of the intermittent abdominal pain, she was readmitted to the hospital.

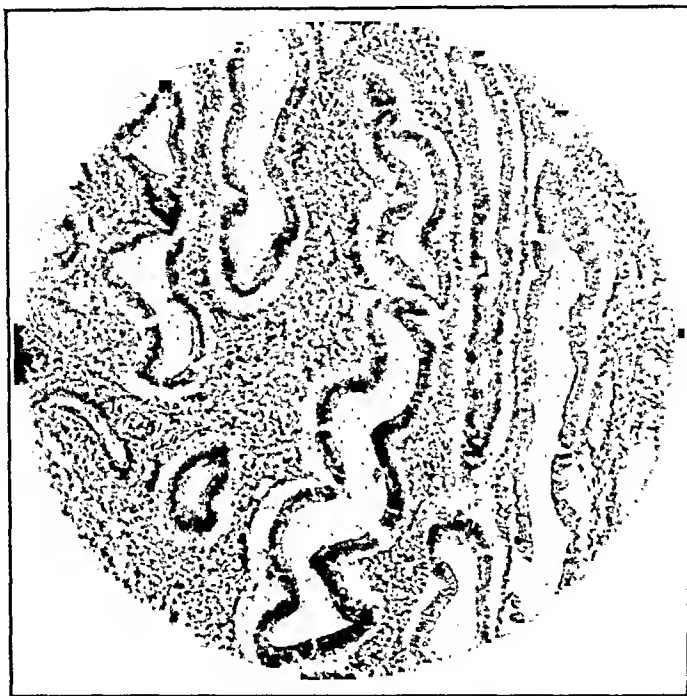


Fig. 1.—Endometrial proliferation of tortuous and dilated glandular acini (low magnification).

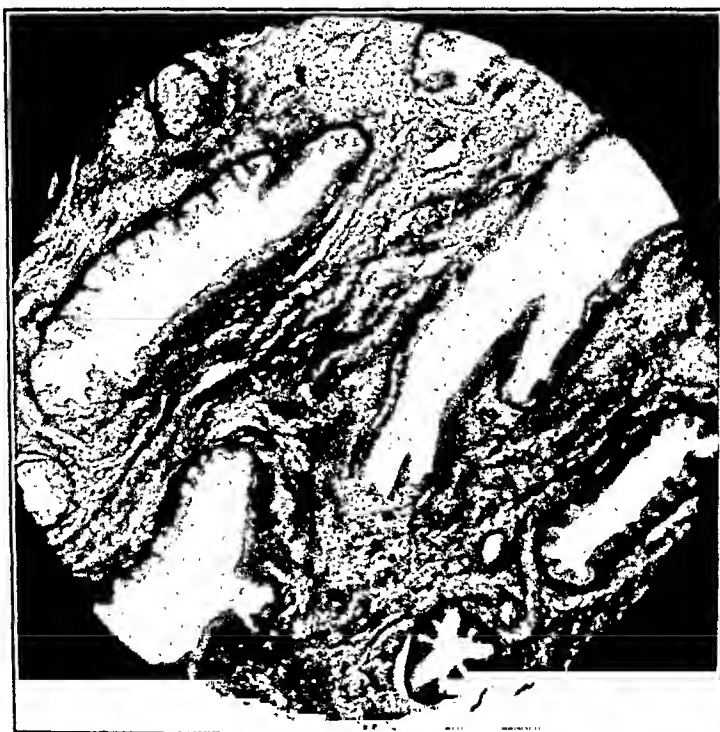


Fig. 2.—Cervical glands showing a typical hyperplasia (low magnification).

At this time, after no apparent loss of weight, the pelvic examination revealed a rather smooth oval-shaped mass arising from the right lower quadrant extending to the umbilicus. The red blood count was 3,920,000, hemoglobin 65 per cent,

Tallqvist, the white count 12,480, and the differential count 80 per cent polymorphonuclears, 14 per cent lymphocytes, and 6 per cent large monocytes; other laboratory work was essentially negative.

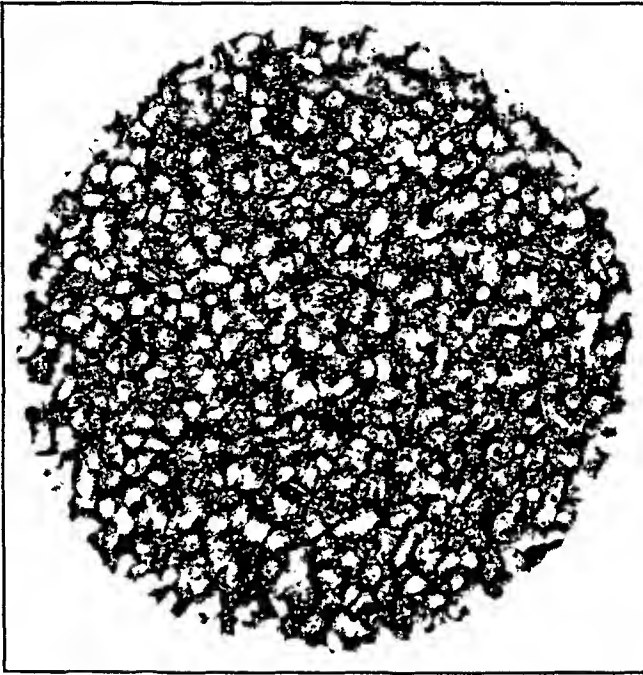


Fig. 3.—Solid mass of granulosa cell tumor (high dry magnification).

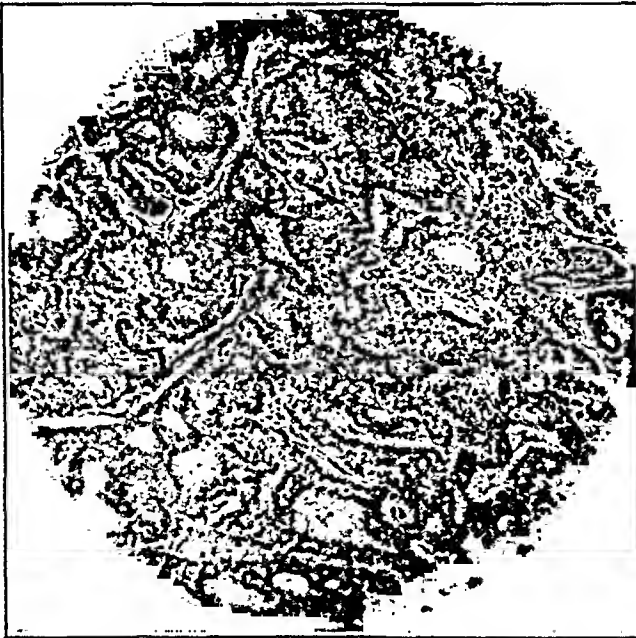


Fig. 4.—Folliculoma associated with cysts. Section taken at random (low magnification.)

A clinical diagnosis of ovarian cyst was made and on May 2, 1933, the patient was subjected to a right salpingo-oophorectomy with the delivery of a mass, the size of a honeydew melon.

Pathological Report: The tumor measured 26 by 22 by 16 cm. in its largest axes. The surfaces were smooth, grayish white and markedly lobulated. On section, the

exposed surfaces revealed numerous roughly nodular areas sharply separated by thick or thin fibrous septa. These areas varied from 0.3 to 5 cm.; their texture was coarse or finely granular and their color was pearly gray or yellow. Interposed in the bulk of the tumor were several hemorrhagic cysts varying from 0.2 to 8 cm.

The tube was without gross abnormality and microscopically showed an atropic mucosa with a spotty lymphocytic infiltration of the submucosa with moderate fibrosis of the muscularis.

After fixing in 10 per cent formalin, the tissue was stained with hematoxylin eosin.

Microscopic Description: Sections showed a fibrous or fibromyxomatous stroma invaded by well-defined nodular masses composed of large polyhedral cells devoid of cellular membrane, with a clear, granular foamy cytoplasm with centrally placed round or oval nuclei moderately dotted with chromatin granules. Nuclear vacuolization was often seen. The nucleoli were conspicuous. Mitotic figures were infrequently found. The epithelium had a varied arrangement. The bulk of the tumor

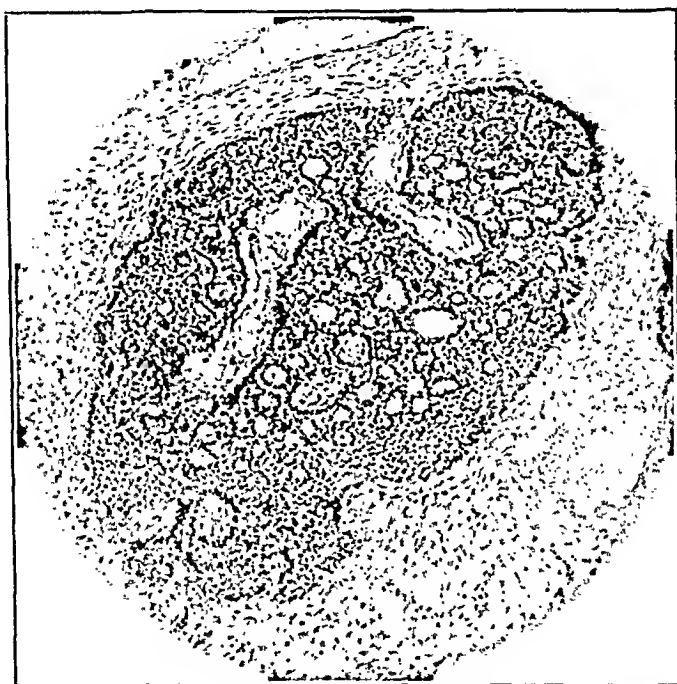


Fig. 5.—Folliculoma associated with cysts. Section taken at random (low magnification.)

was composed of solid masses of granulosa cells, although not infrequently, these cells were supported by a hyaline stroma. In places, the epithelium assumed a cord-like appearance which resembled the undifferentiated gonadal structures.

In other areas, a follicular arrangement of the epithelium, with simple or hemorrhagic cystic degeneration, was noted. Vascularity was poor and some of the medium-sized vessels manifested subendothelial proliferation, leading to partial or complete occlusion of the lumina.

CONCLUSIONS

1. Vaginal bleeding, in the absence of tumors of the uterus or cervix, should suggest, among other possibilities, a granulosa cell carcinoma.

2. Granulosa cell carcinomas, as a rule unilateral, have a low degree of malignancy and the prognosis, after removal, is good. (At the time of writing, our patient is still in good health.)

3. The hormonal influence of these tumors is typically illustrated by this case.

TUBAL PREGNANCY IN A CASE OF BILATERAL TUBAL IMPLANTATION*

WITH INSPECTION OF OPERATIVE SITE AFTER THREE YEARS

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FOR the past few years at Bellevue Hospital, we have been doing plastic surgery upon occluded oviducts according to the technic described and published by us in 1932.[†] We therefore believe this case report is of interest for the following reasons:

1. A celiotomy permitted a survey of the end-results of the tubal implantation technic.

2. The tubal patency persisted postoperatively for a period of years, and there was no evidence of contraction due to cicatrization of the newly created ostia in the horns of the uterus upon the implanted tubes.

3. Intrauterine gestation has occurred following plastic operations on the oviducts, as we reported, but the possibility of ectopic pregnancy must also be borne in mind; not primarily the result of the operation, but most probably of pathologic damages in the occluded tubes which remain from the original disease, if we are to accept the theory of infection as the main etiologic factor in tubal pregnancy.

Mrs. I. K., aged thirty-one years, was hospitalized because of severe right lower quadrant pain and backache of six months' duration. She was operated upon in February, 1932, for chronic adnexal disease and a retroverted, adherent uterus, with both adnexa prolapsed and adherent in the culdesac. No definite history of any previous infection could be obtained.

Operative Findings: Uterus retroverted, adherent in culdesac, with a fibroid, 1 cm. in diameter, on the fundus, 2 cm. from the right cornu. The omentum was adherent to its posterior surface. Both adnexa were prolapsed, the left being adherent; both ovaries appeared to be normal.

An intrapelvic tubal insufflation test disclosed that both tubes were occluded about 0.5 cm. from the cornu. Because the patient had never been pregnant, it was decided to perform a plastic operation upon the tubes. Therefore, both tubes were implanted into the uterus according to the technic referred to. An Olshausen suspension of the uterus was done. The small subserous fibroid was enucleated. Both adnexa were suspended, using the Poole technic.

The convalescence was uneventful.

Three weeks after discharge from the hospital, the uterus was in good position and no adnexal pathology was palpable. A transuterine tubal insufflation demonstrated the patency of the tubes.

For the following seventeen months the patient was symptom free, and her menses were regular. She then had an amenorrhea of seven weeks' duration. After strenuous daily indulgence in swimming during this entire period of amenorrhea she started to bleed, and her local physician diagnosed the case as one of intrauterine pregnancy with abortion and treated her palliatively, no curettage being deemed necessary.

*Presented at a meeting of the New York Obstetrical Society, February 11, 1936.

†Holden, F. C., and Sovak, F. W.: *AM. J. OBST. & GYNEC.* 24: 684, 1932.

After this abortion her menses again were regular, every twenty-eight days, with no associated pain, until one year later (about July 18, 1935), at which time following a six weeks' amenorrhea, she complained of a gradually increasing vaginal bleeding accompanied by occasional abdominal cramps of fourteen days' duration. On Aug. 2, 1935, the abdominal cramps became severe and localized in the right lower quadrant, associated with vomiting and a feeling of weakness, but no fainting.

Examination at this time revealed marked tenderness and slight rigidity of the lower abdomen, with a tender mass palpable in the right lower quadrant just above Poupart's ligament. Vaginally there was a dark, bloody discharge; the cervix was in good position; the fundus well anterior, slightly enlarged and soft. There was extreme tenderness in the uterosacral region, and a fixed, tender mass in the right adnexal area about 8 by 10 cm., extending into the culdesac. Pulsating vessels were also palpable. The left adnexal region was negative.

Clinical Findings: Hemoglobin 55 per cent (Sahli), erythrocytes 2,800,000, with 12,000 leucocytes, differential count 70 per cent polymorphonuclear cells, 15 per cent lymphocytes, and 5 per cent monocytes. The blood pressure was 100/80. The temperature was normal, but the pulse was 105.

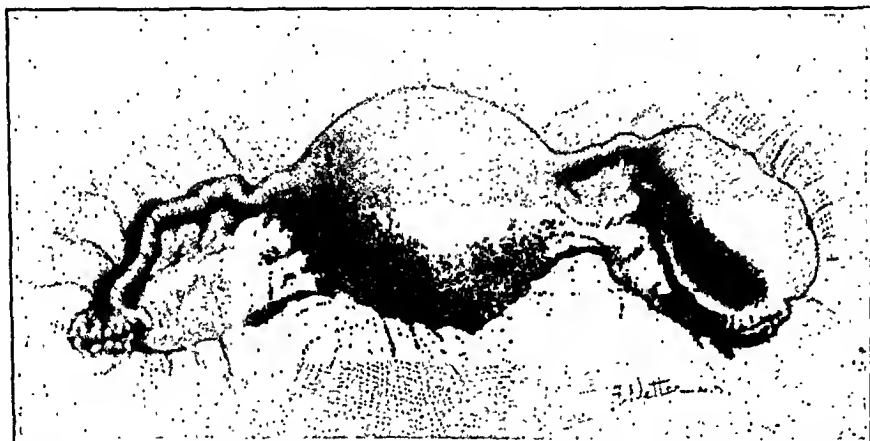


Fig. 1.—Left implanted tube appears practically normal although slightly shorter. Right tubal pregnancy in fimbriated extremity of tube. Left tube found patent by intratubal insufflation test.

A diagnosis of tubal abortion was made and a celiotomy was advised.

Operative Findings: Many free and partially organized blood clots were found in the peritoneal cavity. The right tube was edematous, bluish and distended in its outer half by a mass 3 by 6 cm., with free blood oozing from its fimbriated extremity. The right ovary showed a corpus luteum cyst and was adherent to the tube. The left tube and ovary appeared to be grossly normal and well suspended by the previous Poole technic. The uterus was well anterior, slightly enlarged and soft.

Operative Technic: The old suprapubic scar was excised. The blood and blood clots lying free within the peritoneal cavity were removed and a right salpingectomy was performed. The left tube was then insufflated and found to be patent; no definite cicatricial tissue was identified about the left cornual portion of the uterus, and the implanted tube appeared as if it were a tube in its normal position except that it seemed to be slightly shortened. No evidence of adhesions or kinking was present.

The patient had a mild postoperative reaction and was discharged on the tenth day.

Pathological Report: "Gross specimen consists of a distorted tube about 8 cm. in length and 3 cm. in diameter in its entire outer half, with thickened, congested, and edematous walls. The fimbriated end was retracted. Accompanying the specimen were remnants of blood clots which appear to be partly organized.

"Microscopic section of the tube shows the walls congested, edematous and hemorrhagic, showing abundance of cellular infiltration mostly of polymorphonuclear leucocytes which is most abundant in the mucosa. The tubal blood clot shows groups of decidual cells and chorionic villi."

Diagnosis: Tubal ectopic gestation.

CONCLUSIONS

Although ectopic tubal pregnancy may ensue in oviducts that suffered from infection, normal intrauterine gestation occurs often enough to justify plastic operations upon the tubes.

755 PARK AVENUE

PREGNANCY AND DELIVERY AT TERM FOLLOWING RECONSTRUCTION OF OVIDUCTS*

FREDERICK C. HOLDEN, M.D., F.A.C.S., NEW YORK, N. Y.

MRS. M. C. H., aged thirty-three years, married four years; chief complaint: sterility. Past medical history: diphtheria and typhoid fever. Past surgical history: 1921 laparotomy for acute appendix with abdominal drainage. This was followed ten days later by a posterior colpotomy with drainage of a complicating pelvic abscess. Menstrual history: onset thirteen years, twenty-eight-day interval, duration seven days, moderate flow with very little pain. The physical examination was negative except for a firm McBurney's scar. Normal marital introitus, Skene's ducts and Bartholin's glands negative, cervix in axis and canal clean, uterus normal size and in third degree retroversion, not replaceable. No adnexal nor parametrial pathology palpable.

Several attempts at tubal insufflation showed no gas passing through at pressure up to 200 mil. of mercury. Lipiodol examination was done June 20, 1933. This showed both tubes closed at the fimbriated extremities and no lipiodol escaped into the peritoneal cavity subsequent to the test.

The husband was thirty-three years old, height 5.7, weight 159, general health excellent. Sperm examination showed the number to be adequate and of good motility. Morphologic examination showed 90 per cent normal heads, indicating the sperm to be well within the normal limits of fertility.

A laparotomy was done July 12, 1933, at the French Hospital. Operative findings: The uterus was adherent in retroversion, and both adnexa were buried behind the uterus. The left tube was transformed into a hydrosalpinx which still contained some lipiodol. The left ovary was normal. The right tube and ovary formed a firm inflammatory mass, which was densely adherent to the culdesac and pelvic peritoneum, the ovary being enlarged to three times its normal size. Both tubes were closed at the fimbriated extremities. Many adhesions were present at the site where the appendix had previously been removed.

Operative technique: A phimosi operation was done on the end of each tube according to the Bouney-Sovak technic, leaving both tubes patent at the end of the operation. A Webster-Baldy suspension of the uterus and Poole's suspension of

*Read before the New York Obstetrical Society, February 11, 1936.

both ovaries were done. The abdomen was closed without drainage. On the third postoperative day, a Rubin test was done and gas flowed through the tubes at 20 mm. of mercury. From the fifth postoperative day until discharge, daily Elliott treatments were given. The patient had a smooth postoperative course and was discharged on the fifteenth day.

A Rubin test done two months after the operation showed both tubes to be of normal patency. For eight months after the operation the husband was away on business. The patient became pregnant six months after his return. She was delivered at full term of a normal male child Sept. 30, 1935, and had a smooth postpartum course.

DISCUSSION

DR. THOMAS C. PEIGHTAL.—The percentage of subsequent tubal patencies in any series depends largely upon the choice of cases suitable for this operation. Even on an active service the number of such cases is not large. During the past three years on the Gynecological Division of the Roosevelt Hospital in only fifteen instances has the condition of the tubes been found favorable for implantation into the uterine cornua. This has been done by the Sovak method and in approximately 80 per cent subsequent patency has resulted.

Unfortunately in none of these cases has pregnancy ensued. The physiologic efficiency of these reconstructed tubes must necessarily be greatly reduced by the preexisting mucosal damage so that the obtaining of patency is only part of the problem in overcoming the sterility. Based upon patency alone, these operations have achieved a higher degree of success in our hands than any reconstructive surgical procedure heretofore practiced, and on this basis alone can be recommended to patients with assurance. However, if the ultimate success of these operations must be judged by the pregnancies obtained, it would seem that the problem of sterility from chronic salpingitis is only partly solved.

DR. ISIDOR C. RUBIN.—In my experience, success comes more readily in the cases where the fimbriated ends of the tubes have become agglutinated from an infection gravitating downward from a suppurative appendicitis. I have had several such cases where the tubes, being sealed like a phimosis, have yielded to an insufflation pressure of from 160 to 200 mg. of mercury. Pregnancy has occasionally taken place as a result of that treatment. The cases of gonorrheal infection, however, where the occlusion takes place at the isthmie portion, are not so favorable.

Success is more likely to follow a combination treatment which considers not only the mechanical occlusion but also the fact that the tubes themselves still contain residual inflammation.

I would like to ask Dr. Sovak whether he has met with intrauterine gestation continuing to term after the tubal implantation operation. I myself have done this operation several times and have had no such success.

DR. H. DAWSON FURNISS.—There is a point in the technique of the implantation of the tube that I think serves to simplify the operation. This consists in passing a Reverdin needle through the fundus into the end of the cork borer after the borer has reached the uterine cavity. When the borer is removed the needle will be found protruding from the tunnel that has been cut. A suture that has been passed through the end of the tube is threaded into the needle. Withdrawal of the needle and traction on the suture will pull the tube into the uterine cavity.

DR. SOVAK (closing).—As we know, many other factors besides the mechanical ones enter into the question of sterility. Bilateral occlusion of the tubes, however, stigmatizes the woman as being absolutely sterile instead of relatively sterile.

In answer to Dr. Rubin, I would state that in our first case of implantation done at Bellevue Hospital, the patient became pregnant. This case was one of the first series that we reported.

At the Bellevue Hospital out of 15 implantation cases, we could follow only 10, and of these 10, 6 were found to have patent tubes. The cases that Dr. Holden and I reported tonight were private cases. If we follow only our private cases, the results will show marked improvement over the hospital series.

DR. HOLDEN (closing).—One should not consider operating for occlusion of the tubes without definite information as to the general health of both wife and husband, including a morphologic sperm count. Our statistics demonstrate that in over one-third of the sterile couples, the husband is the cause of the infertility.

Within one year we have seen three doctors' wives, one with secondary and two with primary sterility, in all of whom the husbands had poor sperm specimens. After these husbands had been put in better condition, the wives became pregnant, two delivered full-term healthy babies, and the third had a six months' miscarriage. Many miscarriages and congenitally deformed children can be traced to poor sperm.

CHORIONEPITHELIOMA COMPLICATED BY SEPTICEMIA*

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A WHITE multipara, aged forty-one years, married, gave a history of pericarditis during childhood. Her menstrual history was essentially normal. She was married at twenty-six years and has three children living and well, the youngest nine years of age.

There were at least two uncomplicated abortions. In June, 1935 the last normal menstrual period occurred. Six weeks later profuse bleeding started, but there was no evidence of the patient having been pregnant. A show of blood continued throughout July and August but in September this stopped for about two weeks. The husband reported that a pelvic examination in August showed the organs to be in normal condition. Late in September the bleeding recurred so that early in October she was again examined and a small mass was palpated in the region of the right adnexa. Subsequently I learned that a Friedman test was positive on October 4.

My first contact with the patient was on October 7. She had no complaints except slight backache and occasional bloody discharge. Examination was essentially negative, except for the palpation of a soft cystic mass the size and shape of the average thumb located in the right broad ligament region extending down to about the level of the tip of the cervix. A diagnosis of broad ligament cyst, ectopic pregnancy, or chorionepithelioma was ventured. Because of the age of the pregnancy and freedom from pain the diagnosis of ectopic was ruled out. The latter diagnosis, namely chorioma, was considered most seriously.

Diagnostic dilatation and curettage were immediately advised, but the patient did not enter the hospital until October 14. The small uterus was deeply and carefully curetted and yielded only a very atrophic endometrium in the early proliferative phase. The mass in the right vaginal wall appeared slightly bluish and vesicular and suggestive of dilated veins. A piece of tissue 2 by 1 cm. was excised. Unusually active bleeding occurred which was controlled only by deep sutures. Again the diagnosis of chorionepithelioma was seriously considered, but the pathologist could find no evidence of malignancy and reported the following: "Almost complete disappearance of squamous epithelium, inflammatory reaction, congestion but no decidua reaction."

*Read at a meeting of the Chicago Gynecological Society, January 17, 1936.

The convalescence was uneventful. The patient returned to her home on the fifth postoperative day after an afebrile convalescence. Five days later a very brisk hemorrhage occurred necessitating packing, hospitalization and resuturing of the incised area in the vagina. The tissue had sloughed and the area had increased in size to about 2×6 cm. Spurting arteries were visible. These were ligated and the edges of the sloughed area were freshened and resutured. Eight transfusions were subsequently given.

In one extremely tiny bit of all of this tissue we were able to demonstrate a typical malignant chorioma with marked polymorphonuclear infiltration and hemorrhage.

A Friedman test was markedly positive at this time as was also one diluted 1 to 10 times. However, only one ovary in each rabbit showed the typical hemorrhagic follicles.

Within nine hours following the secondary closure, a fifteen-minute chill occurred followed by daily or twice-daily chills, and elevation of temperatures as high as 107.6° rectally. The pulse varied from 80 to 140. A blood culture was positive for staphylococci. The blood counts both red and white were high but both gradually



Fig. 1.—Tissue from broad ligament showing typical malignant chorioma with polymorphonuclear infiltration.

fell. Convalescent serum and pentose nucleotide were administered. The blood sedimentation velocity was 31, not unusually rapid. There was a severe pyuria.

Slight to moderate vaginal bleeding with a fetid discharge continued necessitating daily packing moistened with 5 per cent mereurochrome. The patient became icteric and toxic.

Consultants agreed that temporarily at least control of the septicemia was most important and that treatment of the chorionepithelioma should be held in abeyance. On the eighth day following the secondary closure a profuse hemorrhage recurred necessitating an attempt at a second resuturing or ligation of the internal iliac vessel. At this time the slough had become so deep it was impossible to reach its apex. The edges were whipped together with great difficulty due to the friable necrotic tissue. However, the bleeding was controlled but again the temperature rose to 108° and within twenty-four hours another severe hemorrhage occurred resulting in death. No attempt was made to ligate the iliac artery due to the extremely serious condition of the patient and apparent rapid extension of the growth.

An autopsy showed an old fibrous scar at the apex of the left ventricle, fresh infarcts in the spleen and two nodules in the right upper lobe of the lungs. These

were 1 cm. in diameter and appeared as soft bluish red masses. Microscopic sections showed that they were thrombosed vessels with metastatic tumor cells, polymorphonuclear leucocytes and tissue which resemble chorionic villi (Fig. 2). The uterus, ovaries, and tubes appeared normal except for a small follicle cyst in the right ovary. The endometrium of the small uterus was very atrophic.

In the right broad ligament there was a mass the size of a baseball. It reached from below the tube to halfway down the vagina. The wall was made up of sloughing, necrotic, hemorrhagic tissue with marked induration. There was extensive thrombosis into the common iliac vein. A thorough microscopic study of this tissue showed no tumor cells.

This case presents many interesting problems. There is the original diagnosis of ectopic pregnancy or chorionepithelioma. The former was never seriously considered because of the duration of the pregnancy and the small size of the mass as well as the absence of pain. Had this been an ectopic in which the fetus had died, the Friedman test should have become negative. It must be admitted that a broad ligament cyst was seriously considered, especially when the uterine curettings and vaginal biopsy showed no evidence of a chorioma.



Fig. 2.—Chorionoma cells in pulmonary vein.

The absence of tumor cells in the uterine curettings, although the curettage was deep enough to obtain uterine muscle, shows the fallacy of ruling out the diagnosis of chorioma by this method. The reason the lesion was not recognized by study of the biopsy material was probably due to the fact that enough tissue was not obtained. The growth was so destructive that all we obtained was evidence of inflammation, hemorrhage, and necrosis.

The severe reaction following the secondary closure was probably due to the absorption of bacteria and necrotic material directly into the blood stream. This made it appear inadvisable to treat the chorioma with radium or x-ray. Of course, surgery was not considered because of the location of the lesion and condition of the patient. Might not it have been advisable even in spite of the bacteremia to have x-rayed this patient?

An interesting feature of the Friedman tests was the reaction to the undiluted and diluted specimens. Only one ovary in each of two different rabbits showed hemorrhagic follicles. This has been observed by others and may be the result of an antihormone, a lack of response on the part of the ovary or a deficiency of hormones. It is difficult to believe that the same ovary in two different rabbits

should be refractory to prolan. Certainly there was sufficient potency, for a dilution of 1-10 produced moderately large blood points. There must be some other explanation.

The most shocking thing about the entire case was the absence of involvement by the tumor of the pelvic organs. Did this lesion reach the broad ligament through the lymph or blood vessels? It probably did so, remained inactive and then took on a very rapid growth months following the termination of a very early pregnancy. Chorionepitheliomas have been found in the testicle, but I doubt if this one had any such anlage. Not until the tumor cells were found in the blood vessels of the lungs did we feel certain that our original diagnosis was correct.

425 EAST WISCONSIN AVENUE

FULL-TERM NORMAL PREGNANCY FOLLOWING THE USE OF ONE THOUSAND MILLIGRAM HOURS OF RADIUM FOR MENORRHAGIA*

HERBERT E. SCHMITZ, B.S., M.D., F.A.C.S., CHICAGO, ILL.

A COLORED female, twenty-three years of age, presented herself at the Cook County Hospital in March, 1935, because of a menorrhagia of one year's duration. Menstruation had begun at the age of twelve years, was always of the twenty-eight-day type lasting five days. Pain or clots had never been experienced. For the year previous to admission the duration of menstruation had been twelve days, very profuse and large clots were passed during the entire period. The previous obstetric and marital history was that she had been married one year and then separated. During the year of married life she had one normal pregnancy resulting in a normal viable fetus. No pregnancies had followed.

Upon admission to the hospital an examination showed a negative introitus, uterus firm but tender in the region of the adnexa, sacral nerve roots and uterosacral ligaments tender. One thousand milligram hours of radium element was advised and the radium inserted on March 11, 1935.

July 15, 1935 the patient presented herself to the Tumor Clinic of the Cook County Hospital with the following history: Last menstrual period Feb. 21, 1935 lasting for twelve days. Following this, radium was inserted on March 11, 1935, and since this time no menses had been noted. Examination at this time revealed an apparently normal colored female. Breasts were enlarged and contained colostrum. Abdomen was negative except for a smooth mass palpable above the pubes. The introitus was negative. Cervix in the midplane and softened. Os round and closed. Fundus size of large grapefruit, smooth but softened. The adnexa were negative. A diagnosis of pregnancy was made. The Friedman test was positive. The Wassermann and Kahn reactions were negative.

The prenatal course was uneventful, life being felt on Aug. 1, 1935. A roentgenologic study Oct. 18, 1935 showed one baby in abdomen with the breech in the pelvis and the spine on the left side. On Dec. 2, 1935, another roentgenogram showed the head in the pelvis and the spine on the left side anteriorly.

Labor began at 5 A.M. on Jan. 2, 1936 and ended Jan. 3, 1936. Duration of the first stage was twenty-two hours; of the second stage, one and one-half hours, and of the third, twenty-five minutes, a total labor of twenty-four hours. The membrane ruptured at 4 P.M. Jan. 2, 1936. It was a normal left occiput anterior. Patient was discharged on Jan. 10, 1936.

The baby weighed $5\frac{1}{2}$ pounds and was perfectly normal in all respects and on discharge from the hospital had regained its normal birth weight.

*Read at a meeting of the Chicago Gynecological Society, January 17, 1936.

UNRUPTURED INTERSTITIAL PREGNANCY*

BEATRICE E. TUCKER, M.D., CHICAGO, ILL.

INTERSTITIAL pregnancy is sufficiently rare to merit the report of the following case. Mrs. F., aged twenty-eight years, was first seen in the office, Dec. 24, 1935. The chief complaints were: intermittent attacks of profuse vaginal bleeding since November 2 and cramplike pain in the left lower abdomen.

The patient had been married three years and had practiced birth control until September, 1935. At this time she wished to become pregnant. Her menstrual periods had always been very irregular, occurring from sixty to ninety days apart, and for the first two days of each period she had been confined in bed with severe abdominal cramps. The last menstrual period was September 1. The surgical and venereal histories were negative. Five years ago she had an attack of nephritis.



FIG. 1.

The onset of the present difficulty was November 2, sixty days following the last period. At this time she had profuse vaginal bleeding with severe cramplike pain in the left lower quadrant, referred to the left thigh. She flowed heavily for seven days and passed clots at times as large as hens' eggs. She was treated for abortion. However, intermittent attacks of more or less profuse vaginal bleeding accompanied with left-sided pain recurred throughout November and December. On December 24 she was referred to me.

At this time general examination was negative except for slight tenderness over the left lower quadrant. The positive findings on pelvic examination were a questionable softening of the cervix and slightly enlarged uterus with a mass about 6 cm. in diameter projecting upward from the left horn. This mass was tense, hard, and tender. A tentative diagnosis of cornual pregnancy or degenerating fibroid was made. The patient was immediately hospitalized for observation.

Upon admission the temperature, pulse, and respiratory rate were normal. The HB 70 per cent, R.B.C. 3,900,000, and W.B.C. 9,200. The urine showed an occa-

*Read at a meeting of the Chicago Gynecological Society, January 17, 1936.

sional hyaline cast. The patient was observed forty-eight hours. She had no vaginal bleeding during this time but complained of some discomfort in the left lower quadrant, and this pain was sticking in character and referred to the left thigh.

On December 26 an exploratory laparotomy was done. The uterus was found to be normal in size. A grayish pink, tense mass, 5 cm. in diameter, jutted upward from the left horn. Both ovaries were apparently normal. The tubes were slightly hyperemic.

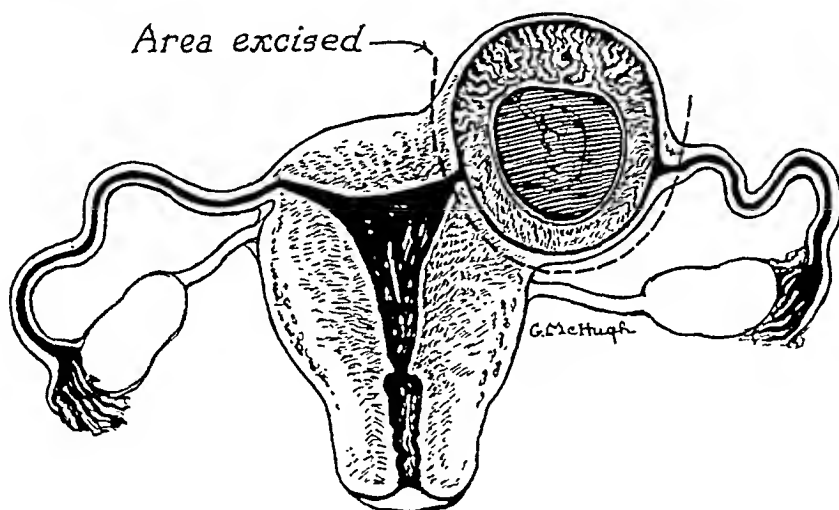


Fig. 2.

The mass was excised by removing a wedge-shaped piece of the uterus and severing the tube. The severed end of the left tube was sewed into the left horn of the uterus and the uterine wall was closed.

The specimen was opened and revealed a fetus 1 cm. long, lying in a gestation sac which dilated the interstitial portion of the tube.

The patient ran a low-grade temperature, from 99-100.6° for five days following the operation. Profuse vaginal bleeding occurred for five days and this ceased after four daily injections of 1 c.c. of antuitrin-S. On the tenth day she was dismissed from the hospital in good condition.

8 SOUTH MICHIGAN AVENUE

Kottneier, H. L.: Results Obtained With Thymophysin in Cases of Uterine Atony, *Acta obst. et gynec. Scandinav.* 14: 382, 1934.

The author reviews the literature on thymophysin and reports his experience with this drug in 163 cases of primary and secondary uterine inertia. Comparing the morbidity and mortality of both mother and child in these cases with a corresponding number of cases of inertia where no oxytocic drugs were administered, he finds that the outlook for the mother and baby was better in the cases where thymophysin was used. He also found that the drug resulted in a decrease in the number of dangerous obstetric operations. On the other hand, thymophysin may result in asphyxia of the child and also the mothers may show untoward reactions. Because of these dangers the author recommends that thymophysin be used only in cases of uterine atony. Not more than 0.5 c.c. should be given at any one time. He could not find any appreciable increase in blood pressure due to thymophysin. The drug is not effective in cases of exhaustion nor is it useful to induce labor. It is ineffective in 10 to 15 per cent of the cases where labor has definitely started. These cases, however, are the ones which should have received the drug earlier in labor.

J. P. GREENHILL

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF FEBRUARY 11, 1936

The following case reports and paper were presented:

Pregnancy and Delivery at Term Following Reconstruction of Oviducts. Dr. Frederick C. Holden. (For original article, see page 346.)

Tubal Pregnancy in Case of Bilateral Tubal Implantation. Dr. Francis W. Sovak. (For original article, see page 344.)

Some Points in the Treatment of Endometrial Hyperplasia by Progesterone Therapy. Drs. Karl M. Wilson, and C. A. Elden. (For original article, see page 194.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF JANUARY 17, 1936

The following case reports and papers were presented:

Unruptured Interstitial Pregnancy. Dr. Beatrice E. Tucker. (For original article, see page 352.)

Full Term Normal Pregnancy Following the Use of 1,000 mg. hr. of Radium for Menorrhagia. Dr. Herbert E. Schmitz. (For original article, see page 351.)

Chorionepithelioma Complicated by Septicemia. Dr. Roland S. Cron. (For original article, see page 348.)

A Study of Fibromyomas of the Uterus With Respect to the Endometrium, Myometrium, Symptoms, and Associated Pathology. Drs. A. E. Kanter, A. H. Klawans, and C. P. Bauer. (For original article, see page 183.)

The Le Fort Colpocleisis. Dr. Fred L. Adair and Dr. Laura DaSef. (For original article, see page 218.)

Acute Nephritis and Pregnancy. Dr. W. J. Dieckmann. (For original article, see page 227.)

Cervicitis and Endocervicitis in Relation to Gynecologic Symptomatology. Dr. Howard J. Hollaway. (For original article, see page 304.)

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Eclampsia and Other Toxemias of Pregnancy

McIlroy, Louise: The Toxemias of Pregnancy. I. Clinical and Biochemical Investigation, *Lancet* 2: 227 and 291, 1934.

Since only six physiologists have taken particular interest in the study of human metabolic function in pregnancy, obstetricians have had to do most of these studies. Toxemias are the second most frequent cause of maternal deaths and produce damages beyond means of estimation. It is impossible to indicate in any way the number of fetal and neonatal deaths as the result of toxic conditions in the mother.

The ovum is the primary etiologic factor. If the ovum fits into its surroundings harmoniously, all goes on to a happy ending. If the adjustment fails, the ovum acts as a parasite and tends to poison its hostess. Theories and predisposing causes of toxemia are mentioned. The diet plays an important part, especially the amount of salt. Salt should be restricted if any untoward symptom develops. Obese or heavy women should keep their weight down, and those who grow too rapidly must also restrict their diet. To combat the retention of tissue fluids, salt must be restricted. Reasonable walks of two to three miles in fresh air are urged.

The toxemias are divided into the hepatic and nephritic groups. The former are often acute and include fulminating eclampsia, acute yellow atrophy, or severe vomiting of early pregnancy. The liver is concerned with the neutralization of protein substances, and when the organ is injured, this function is limited or destroyed. The nephritic type covers two groups: in the one the kidney appears to recover and remains healthy until a second pregnancy, known by some as the low reserve kidney. The other group comprises chronic nephritis. Even with these divisions it is often difficult to make a differential diagnosis.

Some discussion is advanced for toxemia as a deficiency disease. The substances considered are calcium, vitamin D, glycogen, iron, manganese and magnesium, iodine, and even insulin.

H. CLOSE HESSELTINE.

McIlroy, Louise: The Toxemias of Pregnancy. II. The Significance of Symptoms and Their Treatment, *Lancet* 2: 345, 1934.

Emphasis is placed upon treating the patient and not the disease. Prevention is obviously the best approach, even though there are a few fulminating toxemias. In general, the diet should avoid excessive or unsuitable foods. The elimination of harmful substances by physiologic rest and the stimulation of those organs concerned with excretion is necessary therapy.

The diet should be, as far as is expedient, that to which the patient is accustomed. It should be plain mixed variety containing ample vitamins, minerals, and not excessive meat. Constipation should not be treated by cathartics. For morning vomiting confine the patient in bed, allay worries and unusual mental and physical stimuli. For the first twenty-four to forty-eight hours permit only water, glucose, and fruit juices. If vomiting occurs, wash the stomach, use sedatives as necessary, and increase diet as tolerated. Heart burn is best treated by dilute hydrochloric acid (15 to 30 drops) during meals. Headaches should not be overlooked.

Hypertension, if it does not respond to treatment, should be treated by termination of pregnancy. Rapid reduction in hypertension by medication is contraindicated. Venesection has an important place in the treatment.

Ocular disturbances must be carefully interpreted and, with presence of hemorrhages, separation of retina or retinitis, termination is indicated.

Anemia is due principally to vitamin and iron deficiency and should be combated. Foods containing iron are to be urged. Blood transfusion may be necessary in severe anemia, toxemia, shock, and sepsis. The treatment of antepartum hemorrhage depends upon the conditions present. Postpartum hemorrhage is treated best by prevention.

Gas and oxygen is a safe anesthetic.

The urine and blood must be examined, and for kidney function tests uric acid is a finer test than urea. Antenatal and postnatal care are very important and are avenues where improvement may be made in obstetrics.

H. CLOSE HESSELTINE.

Fairbairn, John S.: *Prevention and Prognosis of the Late Toxaemias of Pregnancy*, Brit. M. J. 2: 531, 1935

Late toxemias are those occurring after the twenty-eighth week of pregnancy. A true albuminuria and hypertension are constant features. Frequently edema, headache, vomiting, insomnia, cramps, jaundice, or polyneuritis are associated symptoms.

In the field of prevention, strict antenatal observation, including dietary supervision, especially the administration of carbohydrates, calcium and vitamins, is essential. Foci of infection must be searched for and treated. Early signs of disordered metabolism must be recognized and remedial measures instituted. Bed rest, magnesium sulphate, and alkalis are advisable early in toxemic manifestations. Improvement under this regime justifies continuation of pregnancy; failure to improve is an indication for termination.

In spite of the large number of preeclamptic patients who are saved from convulsions by thorough antenatal care, the actual death rate from eclampsia from 1921 to 1931 and since was unaltered. However, the prognosis for the toxemic patient is somewhat better than formerly. Strict supervision is essential. The prognosis of eclampsia depends upon the number and frequency of convulsions. Coma, fever, and jaundice lend a graver outlook. The danger to the fetus is much less in the nonconvulsive than in the convulsive toxemias, and less than in the chronic nephritic conditions.

F. L. ADAIR AND S. A. PEARL.

Courtols, J., and Lecoq, R.: *Toxemias of Pregnancy and Nephritis*, Gynécologie 34: 665, 1935.

Among the true toxemias the authors include hyperemesis gravidarum, eclampsia, obstetrical shock, hydatidiform mole, uteroplacental apoplexy, and post-

operative toxic infectious shock. Excessive vomiting of pregnancy is above all a syndrome of malnutrition, hypotension, and hypochloremia in which an abnormality in intestinal function plays a large part.

Eclampsia or convulsive and hemorrhagic toxemia is essentially a syndrome of plethora, hypertension, and hyperchloremia with acidosis.

Obstetric shock manifests itself particularly in plethoric women and may be prevented.

In addition to the true toxemias, the authors list a number of "paratoxemias" such as polyneuritis of pregnancy, chorea gravidarum, tetany, osteomalacia, pernicious anemia, icterus gravis, the toxic dermatitis, cardiac accidents and severe forms of the grip.

Nephritis may give rise to symptoms of toxemia. Occasionally it may terminate in eclampsia. Hypertensive nephritis may provoke uteroplacental apoplexy, the hemorrhagic form of eclampsia or obstetric shock.

J. P. GREENHILL.

Strauss, M. B.: Observations on the Etiology of the Toxemias of Pregnancy, *Am. J. M. Sc.* 190: 811, 1935.

In 20 cases of nonconvulsive toxemia of pregnancy the average osmotic pressure of the plasma proteins was 215 mm. of water, in 10 cases of eclampsia it was 175 mm. and in 20 normal pregnant women with adequate diets it was 258 mm. In 15 normal pregnant women who had partaken of diets low in protein, the average osmotic pressure of the plasma proteins was 232 mm. of water.

The average venous pressure in 20 normal pregnant women during the last two months of pregnancy was 10 cm. of water (range 3 to 18 cm.), and in 20 patients with nonconvulsive toxemia of pregnancy 13.3 cm. (range 8 to 20.5 cm.), values which are at least twice as high as average figures for normal nonpregnant subjects.

The dietary histories of 20 toxemic pregnant women showed a low protein intake, probably less than 50 gm. per day, frequently over a period of years.

Fifteen women suffering from toxemia of pregnancy were treated by means of a diet containing 260 gm. of protein, 150 gm. of carbohydrate, and 70 gm. of fat. Ten also received parenteral injections of a vitamin B₁ concentrate and solution liver extract-Lilly (N. N. R.), the latter because of its content of the pellagra-preventive portion of the vitamin B complex. Each of the 15 women showed a loss of weight readily attributable to decrease of occult or gross edema, together with a gradual disappearance of the signs and symptoms of toxemia. No fetal mortality occurred after treatment had been instituted.

Five similar pregnant women suffering from toxemia were treated by means of a diet of approximately equal caloric value, containing 20 gm. of protein, 400 gm. of carbohydrate, and 65 gm. of fat. No significant loss of gross or occult edema occurred. Two of the patients became decidedly worse during a period of two weeks.

It is believed that a manifestation of toxemia of pregnancy is water retention. This water retention probably occurs as a result, among other factors, of a lowered osmotic pressure of the plasma proteins, usually in the presence of an increased venous pressure. The results recorded in this paper suggest that a restricted dietary intake of protein in pregnancy is harmful, and that no injurious consequences follow the administration of high protein diets to women with toxemia of pregnancy. The beneficial results observed in these patients may well have been due to the large protein intake and to the parenteral administration of accessory nutritional factors.

J. THORNWELL WITHERSPOON.

Rowe, A. W., McManus, M. A., and Riley, G. A.: *The Toxemias of Pregnancy*, J. Lab. & Clin. Med 19: 923, 1934.

This study is concerned with protein metabolism as evidenced chiefly in the levels of blood and urine nitrogen. The results are compared with a previously studied normal group of primiparas. This toxemic group consisted of older women, one-third of whom were in their first pregnancy. The authors summarize their work as follows: Pregnancy causes a lowering of the nitrogenous constituents of the blood, uric acid excepted, which is less marked in cases of toxemia as the renal element is an opposing influence. Termination of pregnancy initiates a return to normal levels, the latter being less rapid in the toxic group. Restoration to normal blood levels follows rapidly on the termination of the pregnancy in both studied groups. No evidence is forthcoming in this study that repeated fetation led to results differing from those characterizing primiparas.

W. B. SERBIN.

de Snoo, K.: *Renal Function in Pregnancy Toxicosis and Eclampsia*, Monatschr. f. Geburtsh. u. Gynäk. 97: 253, 1934.

It is the opinion of de Snoo that in the simple toxicosis of pregnancy there is rarely any marked disturbance in the renal function. Likewise, in cases of chronic hypertension, even in those with outspoken uremic manifestations, the kidney function is little if at all deranged in most cases. However, in women who have recovered from eclampsia, there are serious disturbances in the function of the kidneys both as regards the output of fluids and the urinary products. In these women the urinary output is more quickly recovered than the elimination of proteins. The accumulation of proteins in the blood is harmless, and, therefore, the prognosis is dependent more upon diuresis than upon the nitrogen content of the blood. In many cases of eclampsia the renal function is entirely normal before the onset of convulsions. The effect of convulsions on the kidneys is not specific because the same effects may be observed in patients without convulsions. The renal disturbances are dependent upon vasomotor abnormalities, especially spasms of blood vessels. Even without renal disturbances there may be nitrogen retention due to thirst and vomiting. The nitrogen content of the blood in cases of vomiting of pregnancy is a reliable index of the seriousness of the disease.

J. P. GREENHILL.

Evans, Arwyn: *The Late Effects of Toxaemias of Pregnancy*, J. Obst. & Gynec. Brit. Emp. 40: 1024, 1933.

The author has investigated 76 albuminuric patients four months to four years after discharge from the Maternity Department of the Cardiff Royal Infirmary. Two-thirds of these were found to have after-effects, definite chronic nephritis being found in 12, probable chronic nephritis in 7, and simple albuminuria in 16 patients. However, 13 of the patients had other diseases present to account for the albuminuria. With regard to the remote prognosis the following conclusions were formed: (1) If albuminuria is present before the onset of labor for more than fourteen days, the possibility of chronic nephritis developing is very definitely increased. (2) A systolic blood pressure of 170 mm. Hg or over is dangerous, and when present for any length of time the question of terminating the pregnancy must be considered. (3) Every patient should remain in bed after the birth of the child until the albuminuria has disappeared, unless there is good reason to suppose that the chronic nephritis antedated the

pregnancy. (4) The older the albuminuric patient the more liable she is to develop after-effects. (5) The ultimate prognosis seems to be more favorable in primiparas than in multiparas. (6) A good prognosis may be given the child if he survives the first fourteen days. (7) The situation of the edema, the amount of albumin and presence or absence of casts in the urine do not seem to bear any relation to the remote prognosis.

WILLIAM F. MENGERT.

Gibberd, G. F.: The Significance of Recurrence in the Late Toxaemias of Pregnancy, *J. Obst. & Gynec. Brit. Emp.* 41: 23, 1934.

One hundred and twenty-one women who suffered from a late toxemia of pregnancy were examined at intervals of from two to twelve years after the first toxemia. All of these 121 women were initially healthy, and none was included in the series unless there was positive evidence that she was free from renal disease prior to the first toxemic pregnancy. Thirteen of these 121 women, or 11 per cent, subsequently developed chronic nephritis, and 3 of them died of uremia. Thirty-five, or 38 per cent, had a recurrence of albuminuria with subsequent pregnancies but did not show evidences of permanent renal damage in the nonpregnant intervals.

The author concludes that a first toxemia may affect a previously healthy woman in one of three ways: It may give rise to an obvious chronic nephritis. It may be followed by a more or less habitual recurrence of the toxemia with subsequent pregnancies with apparently normal kidneys in nonpregnant intervals. It may leave the patient absolutely normal.

WILLIAM F. MENGERT.

Cadden, J. F., and McLane, Charles M.: A Study of Various Kidney Function Tests in Relation to the Toxemias of Pregnancy, *Surg. Gynec. Obst.* 59: 177, 1934.

Chronic nephritis is a grave and fairly common complication of pregnancy, although it is one of the most difficult conditions to recognize in its earlier stages. Many tests have been developed for the purpose of detecting the impairment of kidney function. One of the difficulties of interpretation lies in the fact that all of the tests are not based on the same principle. A study has been made of the phenolsulphonephthalein, creatinine excretion, and urea clearance tests in 23 cases of normal pregnancy and in 343 women suffering from some type of toxemia. Only the urea clearance test is sufficiently sensitive to differentiate chronic nephritis from the other toxemias of pregnancy. The lower limit of normal is probably in the neighborhood of 70 per cent normal and the average urea clearance value is 75 and 68 per cent normal for antepartum and postpartum, respectively.

Fifty per cent of all the nephritic patients showed values below 70 per cent normal. There is no apparent relationship between blood pressure and kidney function as measured by the urea clearance test. According to this test, there is no kidney impairment in the low reserve kidney group.

The average urea clearance values for preeclampsia and eclampsia are lower than those obtained in normal pregnancy.

To be assured that one is dealing with a nephritic condition it is essential that repeated two-hour tests be performed.

WILLIAM C. HENSKE.

Picardi, Michele: The Use of Santonin in the Antitoxic Function of the Liver, *Ginecologia* (Torino) 1: 227, 1935.

Picardi states that the antitoxic power of the liver is diminished during pregnancy. Such dysfunction, which is of moderate intensity in normal pregnancy, at term tends to disappear rapidly in the puerperium.

In the toxicosis of pregnancy this test notably shows a hepatic insufficiency in practically all of the cases and in some it was possible to establish a regular curve of elimination parallel to the improvement of the toxemia.

From the studies made with Santonin, the author was able to conclude that this new test for study of the hepatic function can also be used in the obstetric field with great advantage. Moreover, he states that additional to its practical value, it possesses marked simplicity.

AUGUST F. DARO.

Wodon, J. L.: The Experimental Production of Eclampsia by Means of Guanidine Intoxication, *Rev. franç. de gynéc. et d'obstét.* 30: 72, 1935.

The author succeeded in producing eclamptic convulsions by the injection of guanidine. He found the same changes in the acid-base equilibrium of the blood as occurs in eclampsia. He considers this to support the hypothesis which attributes to alterations in the metabolism of guanidine an important rôle in the etiology of eclampsia.

J. P. GREENHILL.

Fauvet, E.: Eclampsia, a Hypophyseal Disorder, *Arch. f. Gynäk.* 155: 100, 1933.

In this extensive and comprehensive study, the author shows that disturbances of water metabolism and balance and of the circulatory system predominate in the edematous, nephrotic and eclamptic syndromes which develop in pregnant and parturient women. The author was able to reproduce all these symptoms, except the convulsive seizures, by administering posterior pituitary extracts to animals.

The pregnant organism undergoes changes which are dependent upon increased hypophyseal function even in health. It is possible that labor is initiated by a hypophyseal hormone, although this is not proved. Anterior hypophyseal hormone is essential for lactation and for growth and development in the newborn. Hoffman and Anselmino have shown that the hypophysis controls the water balance and exchange, and blood pressure and that these substances are increased in eclampsia. Fauvet concludes that the eclamptic syndrome is produced by a pathologic hyperfunction of the hypophysis.

RALPH A. REIS.

Bickenbach, W., and Fromme, H.: Follicle Hormone Content in the Blood of Eclamptics, *Klin. Wchnschr.* 14: 495, 1935.

The authors corroborated Heim's finding of marked increase of follicular hormone in the urine of eclamptic patients. Examinations of the blood of four eclamptic patients by the extraction method failed to reveal any noteworthy increase in follicular hormone over that found in normal pregnant women.

RALPH A. REIS.

Smith, Geo. Van S., and Smith, O. Watkins: Evidence for the Placental Origin of the Excessive Prolapse of Late Pregnancy Toxemia and Eclampsia, *Surg. Gynec. Obst.* 61: 175, 1935.

The serums of women with late pregnancy toxemia and eclampsia have been found to have the same effect upon the ovaries of hypophysectomized rats as the

serums of normally pregnant women. An extract of human placenta also had this effect, while hypophyseal prolactin caused a follicular and luteal activity not caused by any of the other materials tested.

Quantitative analyses have shown that the placentas of toxemic and eclamptic patients contain excessive amounts of prolactin and tend toward low levels of estrin as compared with the placentas of normal pregnancies.

Controls have shown that the liver, spleen, kidney, and fetus contain practically no prolactin or estrin.

It is concluded that the excessive amounts of prolactin previously reported in the blood and urine of toxemic and eclamptic women, as well as the tendency toward low levels of estrin, have their origin in the placenta.

A continued overproduction of prolactin by the placenta is probably a related factor and possibly causal in the etiology of late pregnancy toxemia and eclampsia.

WILLIAM C. HENSKE.

Smith, George S., and Smith, O. Watkins: Further Quantitative Determinations of Prolactin and Estrin in Pregnancy, *Surg. Gynec. Obst.* 61: 27, 1935.

Quantitative studies of prolactin and estrin in 27 cases confirm the previous findings of excessive gonad-stimulating hormone and subnormal levels of estrin in the toxemias of late pregnancy and eclampsia. They also show that an excess of prolactin has probably been present for some time before the appearance of toxic symptoms in cases of late pregnancy toxemia. High levels of prolactin during the sixth and seventh months in apparently normal women may indicate that toxemia will develop, whereas the finding of normal figures favors the prediction of continued normal pregnancy.

Although the highest values for serum prolactin yet encountered have been in cases of eclampsia, the degree of excess of prolactin does not always run parallel with the severity of the symptoms.

WILLIAM C. HENSKE.

Spiegler, R.: What Significance Has Galvanic Irritability in the Detection of Eclampsia? *Monatschr. f. Geburtsh. u. Gynäk.* 96: 280, 1934.

The author found that galvanic irritability is increased during pregnancy, but it is markedly diminished in cases of toxemia. This diminution in electric irritability occurs so regularly that it may be considered an early symptom of eclampsia.

J. P. GREENHILL.

Hurwitz, David, and Bullock, L. T.: Failure to Find Pressor and Antidiuretic Substances in Patients With Toxemia of Pregnancy, *Am. J. M. Sc.* 189: 613, 1935.

Blood was obtained from 1 eclamptic, 7 preeclamptics, 3 pregnant women with hypertension and chronic nephritis, and 3 nonpregnant patients with hypertension. Neither blood pressure raising nor antidiuretic substances were found in these bloods.

J. THORNWELL WITHERSPOON.

Spoljanskij, and Juzelevskij: The Cerebral Pressure in Eclampsia and the Question of Etiology of Convulsions, *Monatschr. f. Geburtsh. u. Gynäk.* 96: 190, 1934.

Manometric measurements of the cerebral pressure in cases of eclampsia were found to be within normal limits. The normal pressure in the region of the cisterna magna in the reclining position goes up as high as 150 mm. water,

while in the sitting posture it is negative. An increase in pressure in the lumbar region does not always indicate an increase in cerebral pressure. A temporary chloroform anesthesia does not lower the cerebral pressure, but the pressure sinks in the region of the subarachnoid space when cerebral fluid is removed, regardless of the site of the withdrawal. The authors could find no confirmation of the theory that an increased intracranial pressure is the cause of eclamptic convulsions.

J. P. GREENHILL.

Eufinger and Weikersheimer: The Influence of Atmospheric Changes on the Incidence of Eclampsia, *Arch. f. Gynäk.* 154: 15, 1933.

The greatest incidence of eclampsia at the Frankfurt Frauenklinik occurred during May and November. Temperature readings, humidity and barometric pressure apparently play no rôle in this series of eclamptic patients observed in a ten-year period. Sudden changes in temperature, however, are apparently causative factors in eclampsia, since 89 per cent of the eclamptic seizures took place on days with such sudden changes. It is probable that they affect the vegetative nervous system of preeclamptic patients and thus tend to throw such predisposed patients into eclamptic seizures.

RALPH A. REIS.

Tottenham: Seasonal Incidence of Eclampsia in Hong-Kong, *Brit. M. J.* 2: 1067, 1933.

Eclampsia is thought to be more frequent in the hot countries and may be associated with an insufficient consumption of water by the patient. Tweedy shows a greater incidence (in Ireland) in cold and damp weather. Tottenham compares the incidence of eclampsia and severe albuminuria in the different months of the year at Hongkong (a semi-tropical place), the winter being cool and dry, and the summer hot and damp. Of the 97 cases reported, 66 occurred during the months of September to February inclusive (when the humidity is always below 80 per cent). From March to September (including the months June, July, and August which have the heaviest rainfall) eclampsia is decreased. However, in the 41 cases of severe albuminuria (other than eclampsia), the condition is perhaps more common in hot weather.

F. L. ADAIR AND IRA BROWN.

Brame, Dorthy D.: A Review of Eclampsia at The University of Virginia Hospital, *Virginia M. Monthly* 62: 513, 1935.

This review covers the period 1925 to 1935, during which time 3,927 patients were seen. Of these, 112 had eclampsia, an incidence of 2.8 per cent of all labors, which is almost three times the incidence generally reported in textbooks. However, only three of these 112 patients had been seen in the prenatal clinic, which suggests that inadequate prenatal care is a factor in the unusual incidence of the disease in that institution. About 40 per cent of the patients were seen in the three spring months and 65 per cent of the patients were primiparas. The incidence of the three types of eclampsia was as follows: Antepartum, 74 per cent; intrapartum 8 per cent; postpartum 18 per cent. The maternal mortality was 15.1 per cent, and the infant mortality rate was 30 per cent. The maternal mortality rate was cut in half when more conservative therapeutic measures were used in the last two years. The cases were classified according to Eden, and it was found that the maternal mortality in the severe group was 30 per cent, in the mild group only 7 per cent.

EUGENE S. AVER.

Hauch, E., and Lehmann, K.: Investigations into the Occurrence of Eclampsia in Denmark During the Years 1918 to 1927, *Aeta obst. et gynec. Scandinav.* 14: 425, 1934.

In the entire country of Denmark during 1918 to 1927 there were 1,286 cases of eclampsia among 737,701 childbearing women, a frequency of 1 in every 571 cases. The authors could not detect any influence of the weather upon the incidence of eclampsia. They believe that primiparity plays a greater rôle than seasonal variations. They offer the same explanation for the great increase in the incidence of eclampsia among unmarried women. The disease seems to be more common among the youngest and oldest obstetric patients. The maternal mortality for the entire country was 15.5 per cent. The authors found that the mortality was influenced by the number of convulsions, the degree of albuminuria, and the height of the blood pressure.

The best results were obtained by means of expectant treatment. The mortality was highest in patients delivered by cesarean section. In the cases where convulsions occurred during labor the lowest maternal mortality was obtained by means of rapid delivery. Almost half of the children born were premature. The entire fetal mortality was 34.1 per cent.

J. P. GREENHILL.

Ross, Robert A.: The Toxemias of Pregnancy and Certain Deficiency Diseases, *Virginia M. Monthly* 62: 424, 1935.

The author noted that in the area (rural North Carolina) from which his clinic practice mainly is drawn, eclampsia occurs most often in the same localities in which pellagra and similar vitamin deficiency diseases are frequently found. On close questioning he observed that the type of patients he saw in eclamptic convulsions subsisted mainly on a diet deficient in vitamin G (B_2), and also vitamins A, C, and D. Ross makes no conclusions from his observations except to state that the pellagra and eclampsia ratio is clearly parallel in North Carolina, and that he is trying to find a factor which may be helpful in the solution of the problem of the prevention of eclampsia.

EUGENE S. AUER.

Fauvet, E.: Clinical Aspects of Eclampsia, *Arch. f. Gynäk.* 157: 139, 1934.

The author believes that abruptio placentae occurs secondarily to nephritis of pregnancy and may terminate fatally with signs of renal insufficiency. In two patients the maximum excretion of urine and rise in blood pressure did not occur for two weeks after delivery. This may have resulted from secondary inflammatory edema of the kidneys. The anuria may be due to compression of the renal parenchyma, and Fauvet believes that the hypertension is an attempt to overcome this compression. The administration of fluids may be a life-saving measure if this compensatory action fails. Such treatment is successful only in threatening anuria as a result of kidney edema. It is not advisable in circulatory failure.

Fauvet also discusses the causes of late puerperal hypertension and believes that this is due to hormonal action of the hypophysis-interbrain system.

RALPH A. REIS.

Correspondence

A Proposed Obstetric Term

To the Editor:

I hesitate to introduce another term to the obstetric profession, but I feel there is a place for the term "incitoduction." It is especially valuable for use by the record librarian.

The term "induction of labor" should be confined to the patient who is not in labor at the time drugs or mechanical means are employed to bring the patient into labor.

The term "incitoduction" could be applied and should be confined to the use of drugs or mechanical means to stimulate labor in a patient who is already in labor.

Under the present classification we have no place nor a term to index this type of patient. We do not really induce labor in these patients, since labor is already started. What we do is to accelerate the time of delivery.

The verb incite is defined as follows: "to impel to a particular action; urge onward," while the verb induce is defined: "to influence to an act; to lead to or produce." Therefore the term "incitoduction" can be very nicely used to indicate that we hasten the time of delivery of a woman either by drugs or mechanical means.

EDWARD LYMAN CORNELL, M.D., F.A.C.S.

Chicago, Ill.

Item

American Board of Obstetrics and Gynecology

The next written examination and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology will be held in various cities in the United States and Canada on Saturday, November 7, 1936.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Bldg., Pittsburgh (6), Pennsylvania. Applications for this examination should be filed in the Secretary's Office sixty days prior to the scheduled date of examination.

Erratum

In Dr. Stein's discussion of Dr. Irving's paper in the July issue, page 48, the first line should read: "At the Michael Reese Hospital," instead of "At the Cook County Hospital."

American Journal of Obstetrics and Gynecology

VOL. 32

SEPTEMBER, 1936

No. 3

Original Communications

A PRELIMINARY STUDY OF THE CYCLIC HISTOLOGIC CHANGES OF THE HUMAN CERVICAL MUCOSA IN THE INTERMENSTRUAL PERIOD*

ANTHONY WOLLNER, M.D., F.A.C.S., NEW YORK, N. Y.

THE cyclic function of the ovary results in the production of two distinct hormones, the action of which governs the physiologic histologic changes in the female genital tract. The hormone action of the developing and ripening follicle initiates new cell formations in the mucous membranes, and the hormone produced by the corpus luteum brings about changes necessary for the nidation of the ovum.

The cyclic histologic changes are most pronounced in the endometrium. Hitschman and Adler¹ were the first ones who subjected the endometrium to a systematic study, and their description of the cyclic events in that structure is universally accepted. Schroeder's² investigations of structural changes during actual menstrual bleeding supplemented our conception of this subject. The description of these findings stimulated a great deal of research work in animals and in the human being in an effort to find evidence of a menstrual cycle in other parts of the genital tract. Diercks³ reported his observations on the human vagina, concluding that a definite cycle occurs. Although this report was followed by contradictory findings by others, Geist's,⁴ and more recently Papanicolaou's⁵ studies substantiate the presence of a vaginal cycle. Novak and Everett⁶ proved that a definite histologic cycle occurs in the human tubal mucosa, although it is less conspicuous than that of the endometrium.

No definite data are available regarding the cyclic changes of the human cervical mucosa. R. Schroeder⁷ and Nurenberger studied the isthmus of the uterus, and found that it participates in the cycle, but they contend that the cervical mucosa

*Read at a meeting of the Section of Obstetrics and Gynecology of the New York Academy of Medicine, February 25, 1936.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

does not show any evidence of definite involvement, and this is now the generally accepted view (Meyer⁸). Novak,⁹ in his recent review of the cyclic histologic changes in the female genital tract, makes the following statement: "Is there a histologic cycle in the cervix? A priori, we would expect that this would be the case, for the cervical mucosa is a derivative of the müllerian epithelium, like the epithelium of the uterus and tube, both of which show such characteristic histologic changes during the cycle. As yet, however, no clear-cut cycle has been described in the case of the endocervix."¹

The investigation of cyclic changes in cervixes of different animals did not yield uniform results. No cyclic change was found in mice and rats (Clauberg¹⁰); on the other hand Hartman and Olbers¹¹ describe a distinct cyclic change of the cervical epithelium in guinea pigs.

Not knowing whether or not the human endocervix takes part in the menstrual cycle makes the proper interpretation of presumably pathologic findings in the cervical mucosa problematical. That the endocervix is often the site of inflammatory changes is indisputable, but whether or not these findings merely represent a certain phase of the physiologic activity of the mucous membrane in some cases is questionable. In the era before Hitschman and Adler's studies, premenstrual congestion and increased glandular activity were considered pathologic and were credited as the basis for irregular bleedings or profuse discharge. Unless the physiologic activity of the endocervix is known, similar errors may also be made in the interpretation of structural changes of the cervical mucosa. If hormonal influence on the endocervix can be proved, changes which are now considered as being due to local pathologic causes might be demonstrated as manifestations of hormone overproduction.

A study of the cyclic changes in the human endocervix presents certain difficulties. A histologic comparison of cervixes after surgical removal or after autopsies would not furnish reliable data. The structure of the endocervix is more subject to individual variations than that of the endometrium.

In an attempt to study the physiologic activity of the endocervix, I employed a method which made it possible to obtain periodically specimens of cervical mucosa from the same patient. In this series of cases two specimens were taken from each patient at two-week intervals. The cutting current of the high frequency machine with the Hyams cervical electrode was used. A detailed description of the instrument, and directions for its proper use, may be found in Hyams' article on cervical conization.¹² The patient does not require any special preparation. She is placed on the examining table, the cervix is exposed with a bivalve speculum, and the portio and cervical canal are wiped dry. The active electrode can be inserted into the canal to the internal os without previous dilatation. The current is turned on, and by a rotating motion of the operator's hand a portion of the cervical mucosa is excised. A stripe approximately 3 mm. wide extending from the external to the internal os is thus obtained and prepared for histologic examination. In some cases there may be a slight oozing from the cervical canal after the procedure, which can always be controlled by simple vaginal packing. No anesthesia is necessary. Some patients experience a burning

discomfort during the cutting, which promptly disappears after the excision has been completed. I never observed any untoward after effects, and the patient may continue her usual activities. In very sensitive patients, surface anesthesia with cocaine or metycaine may be employed. Ten to fifteen days after the first specimen is excised the procedure is repeated and the two specimens histologically compared. Precautions are taken to eliminate possible errors in the histologic interpretation of the two specimens, due to secondary local reaction after the first cutting. The specimens are always taken from two remote corners of the cervix. When the first one is removed from the left upper corner, the second one is removed from the right lower corner. Furthermore, the first specimen is taken preferably in the premenstrual

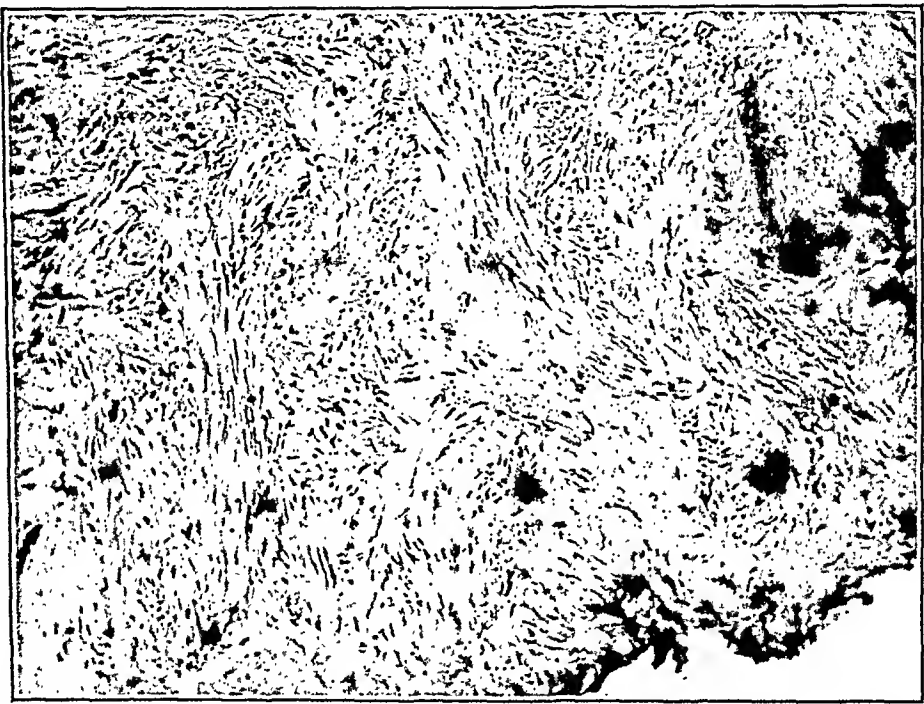


Fig. 1.—Visualizing under high power the postmenstrual stroma characterized by its density.

period, when a physiologic congestion of the tissue is to be expected, and this is followed by the removal of a second specimen in the postmenstrual period.

My observations on nine patients with eighteen specimens form the basis of this study. Eight of the cases were patients between the ages of twenty-seven and thirty-six, all nulliparas, with normal menstrual histories and apparently normal cervixes. In one case observations were made after operative removal of the ovaries.

CASE 1.—A thirty-one-year-old woman, never married, never pregnant, had her first menstruation at the age of fourteen, recurring regularly at twenty-eight-day intervals, three days' duration, moderate bleeding without pains. On vaginal examination, a normal uterus was found in good position, freely movable, adnexa

negative. Through the speculum an apparently normal cervix was visualized. The first specimen was taken twenty-four days after the patient's menstruation. Five days later she began to menstruate, which was the expected date of her next period.



Fig. 2.—Giving the high power picture of the markedly loose and vascularized stroma of the premenstrual phase.



Fig. 3.—Picture of a typical postmenstrual gland under low power. In no portion of this specimen could I get more than two glands in the field under low power.

The second specimen was obtained six days after her first day of menstruation. The histologic study of these specimens revealed a marked structural difference. The postmenstrual specimen showed a dense stroma with scattered small points of

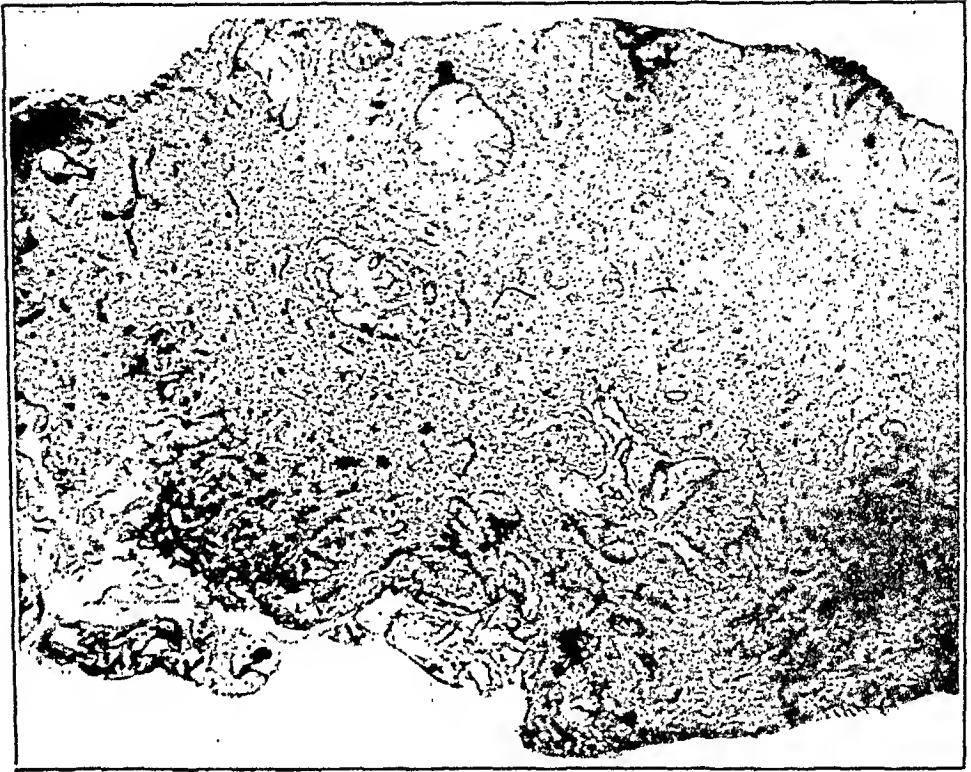


Fig. 4.—Picture under low power, which demonstrates the increase in the number of glands and their variations in size and shape in the premenstrual specimen.

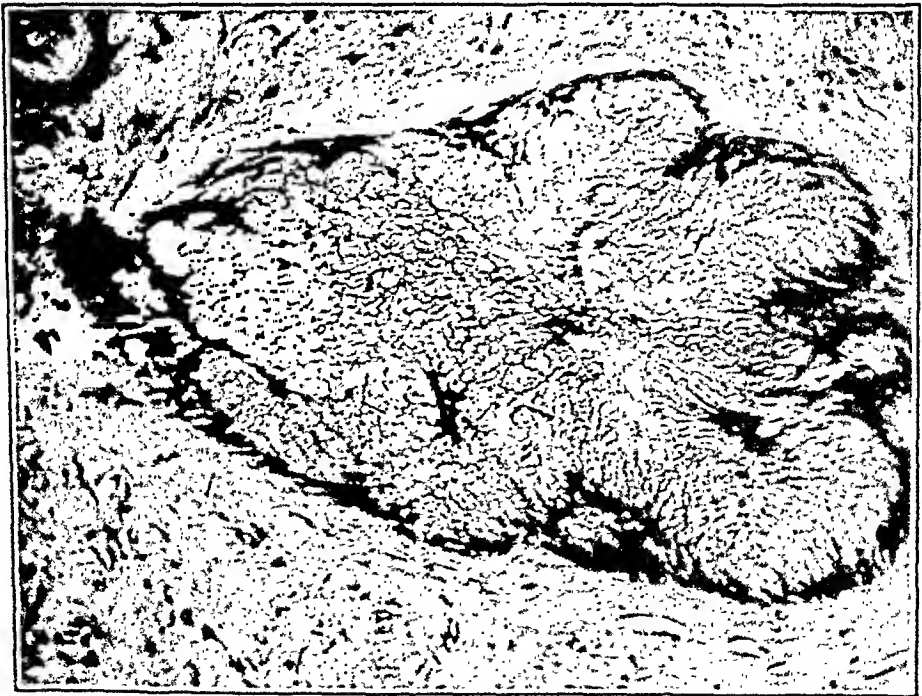


FIG. 5.—Showing the postmenstrual gland under high power. The epithelial lining is low, consisting mostly of one row of cells. There is ample mucus production.

granulation tissue. The glands had a regular outline, were round or oval shaped, and were scanty and widely spaced. The gland epithelium showed little cytoplasm and one row of small nuclei close to the basal line. In the premenstrual specimen, the stroma was well vascularized and contained many engorged small blood vessels. There was an increased cellularity of the entire cervical tissue. The number of glands was considerably larger, and there was a great variety in their shape and size. There was also considerable folding of the epithelial lining and digit-like projections into the surrounding tissue. The amount of mucus in the glands was reduced and more cytoplasm was present. Nuclei were also more numerous and many were cut longitudinally, showing rod shape.

The cyclic histologic changes in this case are demonstrated in Figs. 1 to 6.

CASE 2.—A thirty-five-year-old woman, single, never pregnant. She began to menstruate at the age of thirteen, was always regular at twenty-eight-day inter-

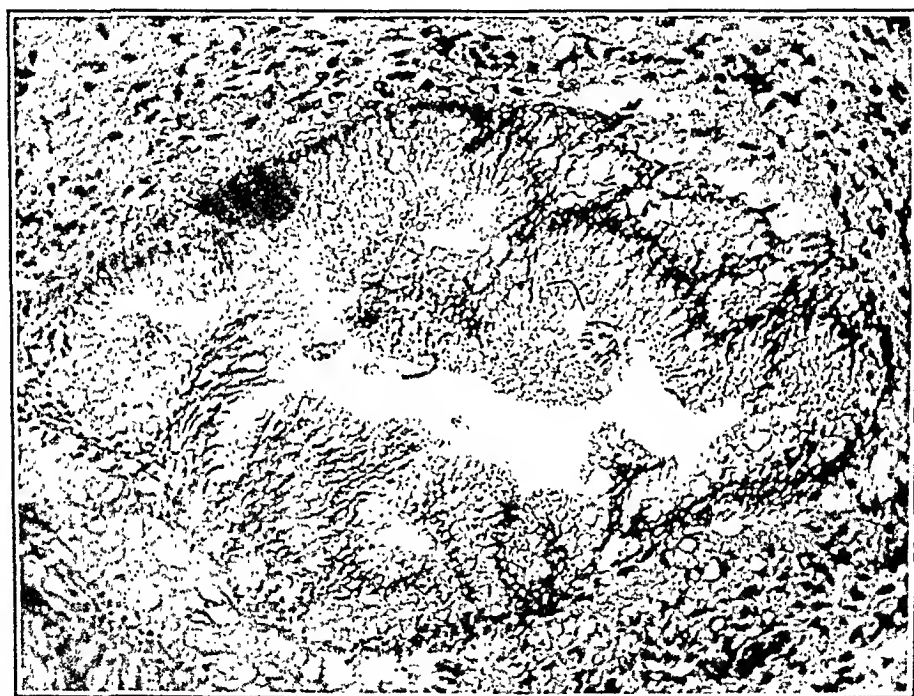


FIG. 6.—Picture of a gland under high power in the premenstrual specimen. There is an evidence of epithelial proliferation in the gland with reduced mucous production.

vals, the bleeding lasting five days, moderate in amount. No history of any genital disease. On vaginal examination a normal uterus and adnexa were palpated. The first specimen was taken fifteen days after the first day of a menstrual period. The histologic findings of this specimen were: the cervical canal was lined by a layer of columnar epithelium with many eosinophiles. The stroma was loose and hyperemic, was infiltrated by leucocytes, mononuclear cells, and eosinophiles. There was a great abundance of glands with folding epithelium and ample mucous production. The nuclei of the epithelium were at the base and in part in the midzone of the cells. The second specimen was taken during the menstrual flow, twenty-four hours after its onset. The histologic picture of this specimen presented a sharp contrast to the first one. The cervical canal was denuded for the most part of lining epithelium. Several layers of exfoliated epithelium covered the surface. The stroma often separated with the epithelium in process of exfoliation. The gland lining epithelium was often in several layers with nuclei at various levels with abundant exfoliation. The exfoliation transformed some of the glands into cysts, prac-

tically without glandular structure. The periglandular stroma was infiltrated by lymphocytes and was edematous where the cervical epithelium was being exfoliated. Figs. 7 and 8 illustrate these changes.

The investigation of four additional cases with eight specimens gave similar evidences of a cyclic histologic process in the endocervix.

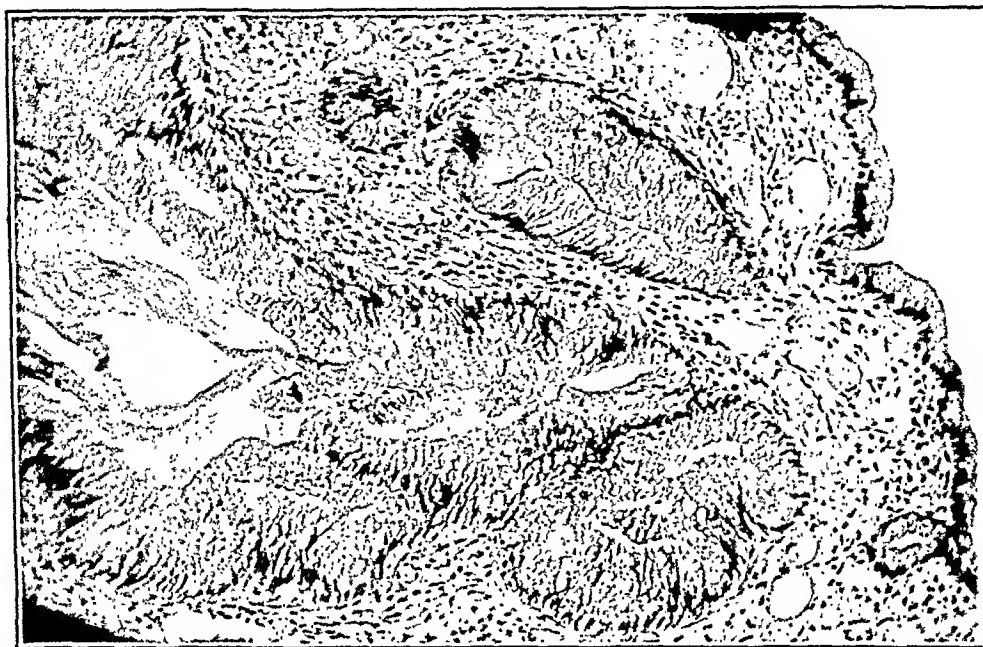


Fig. 7.—Showing the picture of the surface epithelium, stroma, and glands under low power fifteen days after menstruation.

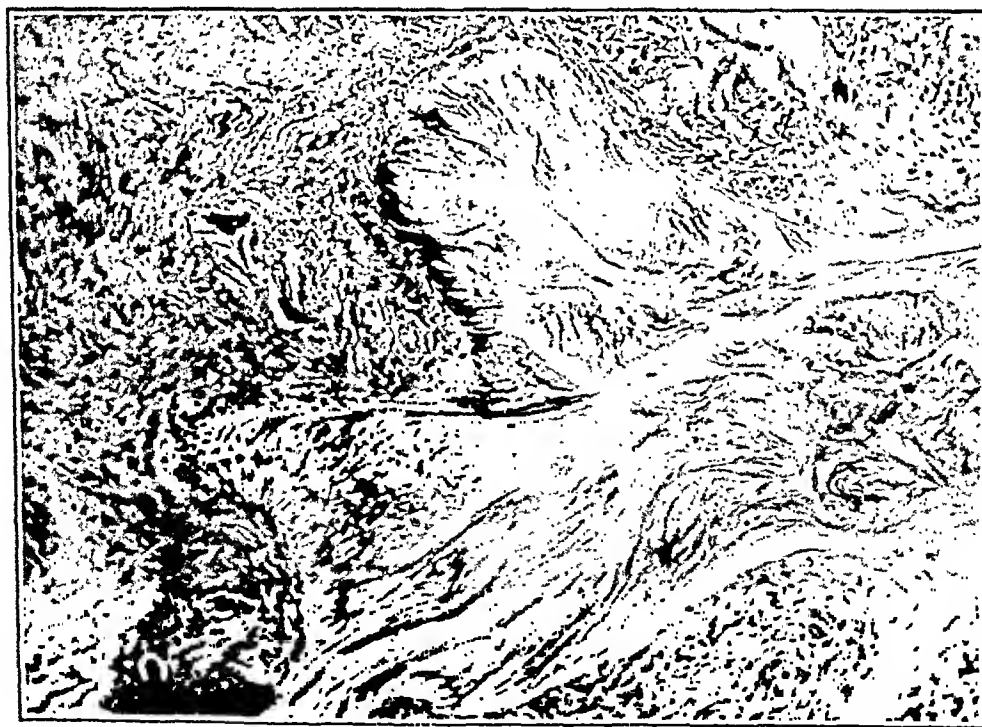


Fig. 8.—High power visualization of a gland during menstruation. Part of the gland is denuded of its lining epithelium. In another part the process of exfoliation is seen and the lumen is filled with exfoliated cells.

In the following case the cervical mucosa was subjected to a periodic study following the operative removal of the ovaries:

CASE 7.—A thirty-two-year-old woman with multiple large fibroids came under observation after a typical supravaginal hysterectomy with removal of the ovaries. The patient made an uneventful recovery and left the hospital on the twelfth post-operative day. Eight weeks later I took a specimen of the cervical mucosa, which revealed atrophic glands surrounded by sclerosed connective tissue. A specimen taken two weeks later gave exactly the same histologic picture. No evidence of any cellular activity could be seen in comparing the two specimens. Fig. 9 gives the low power picture of the cervical tissue in this case. The repeated histologic studies in this case seem to indicate that the removal of the ovaries causes atrophic changes in the cervical mucosa, with complete lack of evidence of glandular stimulation. The observation made on the human endometrium, that the ovary governs the cyclic phases of the mucous membrane, is apparently true also for the endocervix.



Fig. 9.

In two cases of this series no definite cyclic change could be ascertained. In both a more or less constant activity of the tissues was noted, which was only slightly accentuated in the premenstrual period. One of these patients subsequently had to undergo an abdominal operation, which afforded an opportunity to investigate the ovaries histologically in this atypical case, a report of which follows:

CASE 9.—A thirty-one-year-old woman had been married for thirteen years, but had never become pregnant. She always menstruated at irregular intervals, every three to five weeks, with a duration of three to four days' moderate amount of bleeding, with occasional pains during the first two days. Vaginal examination revealed a normal cervix; the uterus was found moderately enlarged, firm, in good position, and freely movable. A small fibroid was palpable in the fundus and another one in the right wall of the corpus. Tubes and ovaries could not be felt. A specimen of the endocervix was taken eight days after the first day of her last menstruation. The histologic findings were the following: there were large and numerous glands present, many of which showed projections into the surrounding

tissue, although others had a perfectly round or oval shape. The nuclei were rod-shaped and fairly numerous. In parts there was a marked exfoliation. The stroma was vascular and edematous in places. The second specimen was taken eleven days after the first one, and five days later the patient began to menstruate. The histologic findings of the second specimen were: the glands were abundant, in part they were hyperplastic and filled with papillas of lining epithelium with nuclei at various levels and with exfoliation. In part, however, the glands were small and compact and were lined by columnar epithelium with deep-staining nuclei at the base and pink staining cytoplasm. The stroma was quite edematous and showed congested blood vessels.

Four months after having examined these specimens, the patient returned complaining of loss of appetite and insomnia. She was worried about her fibroids and insisted on immediate operation.

I therefore performed a supravaginal hysterectomy with removal of the adnexa, twenty-one days after the first day of her previous menstruation. The pathologic report on the extirpated organs was made by Dr. H. L. Meeker: Specimen was a uterus which had been amputated above the cervix, and both tubes and ovaries were attached. The uterus had been opened, disclosing a somewhat edematous and hemorrhagic endometrium lining a canal 50 mm. in length. The myometrium was 22 mm. in thickness, and there was an intramural fibroid 16 mm. in diameter, and beneath the serosa there was a second 20 mm. in diameter. The first tube measured 70 mm. in length, and had a proximal diameter of 4 mm. widening to 12 mm. at the fimbriated end which was free. On section the lumen was patent throughout, and the plicae well formed. The second tube measured 75 mm. in length, had a proximal diameter of 4 mm. and 12 mm. at the fimbriated end which was free. This tube was precisely similar to the first described. The first ovary measured 42 by 27 by 22 mm. It was partly firm, white, and partly bluish and cystic. On section there were several corpora lutea 2 to 3 mm. in diameter. They were filled with reddish jelly. There were also small graafian follicle cysts a few millimeters in diameter, embedded beneath the surface. Second ovary measured 30 by 27 by 22 mm. This contained numerous graafian follicle cysts, the largest 6 mm. in diameter. They were filled with reddish jelly. *Microscopic:* Sections of the uterus including the mucosa showed the endometrium lined by one or two layers of columnar epithelium. The endometrial glands were elongated and tortuous, and some of them slightly dilated and containing coagulated serum. They were lined by several layers of columnar epithelium. The interglandular stroma was relatively decreased but actually hyperplastic. It was very edematous and especially near the surface was suffused with red blood cells, the picture suggesting a premenstrual phase. Sections of the fallopian tubes showed elaborate branching plicae covered by one or two layers of columnar epithelium. The stroma of the plicae was fibrous tissue diffusely infiltrated by lymphocytes and plasma cells, and its many blood vessels contained excess number of polymuclear leucocytes. Sections of the ovary showed numerous small graafian follicles embedded in the cortex. There were also dilated graafian follicles forming the cysts noted in the gross and lined by several layers of epithelium. In addition there were corpus luteum cysts lined by many layers of pale lutein cells. The enclosed blood clot showed beginning organization at the periphery.

In this case the coexistence of an atypical activity of the cervical mucosa with distinct ovarian pathology deserved attention.

SUMMARY

Nine patients were studied with periodic tissue examinations of the cervical mucosa. In six cases evidence of a definite histologic cycle could be determined. In one case, after operative removal of the

ovaries, atrophic changes and inactivity of the endocervix were found. In two cases the presence of a typical histologic cycle could not be established. One of these cases revealed definite ovarian pathology at subsequent operation.

The number of cases is too small to justify a final conclusion on the histologic cycle of the cervical mucosa. The chief purpose of this paper is to suggest a method which permits periodic histologic investigations of the endocervix in patients. It is a simple office procedure, does not require anesthesia, and provided it is done in the absence of any inflammatory process in the genital tract, it is harmless and without unpleasant after effects. It has been my experience that the raw surface in the cervical canal becomes completely epithelialized in about six weeks. A periodic tissue examination, therefore, can be repeated in the same patient at two- or three-month intervals.

Dr. Max Goldzieher, Endocrinologist to the Gouverneur Hospital of New York City, cooperated with me in making the interpretation of the microscopie slides, and I wish to express my thanks for his valuable suggestions.

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116 EAST SIXTY-EIGHTH STREET

Murphy, Douglas P.: Reproductive Efficiency Before and After the Birth of Malformed Children, Surg. Gynec. Obst. 62: 585, 1936.

The reproductive activity of 405 mothers, each having had a congenitally malformed child, is reported with respect to the incidence of miscarriages, stillbirths, and premature births. Of the 405 families, 151 exhibited one or more miscarriages, stillbirths, or premature births. Of the total of 1,732 conceptions in the 405 families, 63.2 per cent ended normally, 23.4 per cent resulted in malformed children, and 13.4 per cent ended in either miscarriage, stillbirth, or premature birth.

Miscarriages, stillbirths, and premature births occurred more often than would be expected by chance in the pregnancies immediately preceding and immediately following the pregnancy which resulted in the birth of the defective child, and less often than would be expected by chance in the remaining pregnancies. Miscarriage, stillbirth, and premature birth occurred most often in the pregnancy immediately preceding that of the defective child.

It is concluded that the birth of a congenitally malformed child may be only one expression of a prolonged decrease in functional reproductive activity, the other expressions being miscarriages, stillbirths, and premature births.

It is suggested that the obstetrician has unusual reason to suspect the possible existence of a congenital malformation in the pregnancy which follows immediately after a miscarriage, a stillbirth, or a premature birth.

WM. C. HENSKE.

THE ACID-BASE BALANCE OF THE BLOOD DURING NORMAL PREGNANCY AND PUERPERIUM*

MARGARET NICE, M.S., JAMES W. MULL, PH.D., EDWARD MUNTWYLER, PH.D., AND VICTOR C. MYERS, PH.D., D.Sc., CLEVELAND, OHIO

(From the Department of Obstetrics [Maternity Hospital] and of Biochemistry, School of Medicine, Western Reserve University)

THE fact that the acid-base balance of the blood may undergo a slight disturbance during normal pregnancy has been recognized for some time. Upon examining the literature, however, one is impressed by the relatively few studies which have been reported dealing with complete acid-base balance changes. This is particularly true for observations extending throughout the course of pregnancy. That is, most of the publications have consisted in a comparison of the results obtained at or near term with those obtained postpartum.

The results of the more recent studies in which a comparison of the antepartum and postpartum acid-base balance changes in normal pregnancy have been made are summarized in Table I. It will be observed that a lowering of the bicarbonate concentration has uniformly been found by all the workers, and this is equally true for the total base concentration where it was determined. The chloride concentration remains essentially unchanged and the pH appears to vary within normal limits.

No explanation can be given at the present time for the lowering of the bicarbonate concentration which is entirely free from criticism. Since there is evidence⁵ that the blood pH (principally colorimetrically determined pH values) is not infrequently in the upper range of normal and in some instances slightly above normal, Muntwyler, Limbach, Bill and Myers,⁶ for want of a better explanation, accepted the view expressed by Austin and Cullen⁷ that hyperventilation is the main cause of the bicarbonate decrease. This view has been subjected to considerable criticism.⁸

The object of the present study was twofold: first, to ascertain how early in pregnancy the acid-base changes of the blood become manifest, and second, since the colorimetric pH values have been questioned, to compare the colorimetric and electrometric pH values in a series of cases.

METHODS

The present work was carried out in series on each of 33 normal pregnant women from the second or third month of pregnancy to the first and second month postpartum. Twelve additional normal pregnancies were studied only during delivery

*For lack of space the extended tabulations cannot be included here but may be found in the authors' reprints.

TABLE I. A COMPARISON OF THE ANTEPARTUM AND POSTPARTUM CHANGES OF THE ACID-BASE BALANCE OF THE BLOOD IN NORMAL PREGNANCY

	NUMBER OF OBSERVATIONS*	pH	HCO ₃ m.Eq.	Cl m.Eq.	PROTEIN m.Eq.	TOTAL BASE m.Eq.	pH METHOD EMPLOYED	AUTHOR AND DATE
Antepartum	55	7.44	20.5	107.6			Colorimetric	Gaebler and Rosene, ¹ 1928
Postpartum	30	7.41	24.2	107.8		146.1		Oard and Peters, ² 1929
Antepartum	12		22.1	103.7	15.2	151.2		Stander et al., ³ 1930
Postpartum	3	7.37	26.0	102.6	17.2	147.0	Electrometric	Dieckmann and Wegner, ⁴ 1934
Antepartum	3	7.34	20.7	104.0	14.1	155.3		
Postpartum	4	7.39	25.4	106.6	16.4	152.6	Colorimetric	
Antepartum	100	7.39	22.1	103.4		153.3		
Postpartum	80	7.39	22.5	103.1		147.1	Electrometric	
Antepartum	120	7.41	22.1	102.8	14.4			
Postpartum	65	7.42	25.3	102.6	15.6	150.0		Present work

In a number of instances the data have been recalculated to terms of m.Eq. The figures given in the table are means, except for data of Oard and Peters, and Stander et al., where averages are used.

*Maximum number of observations.

and hospital confinement. The blood samples for each group of determinations were drawn under oil and without stasis. With the exception of those taken during labor, when the time and preceding exercises could not be regulated, the blood was obtained before the patient had risen or had had breakfast. As soon as the blood had clotted, it was centrifuged and the serum removed without air contact. The pH was determined both colorimetrically at room temperature and electrometrically with the hydrogen electrode at 38° according to the procedures previously outlined.^{9, 10} The estimations of the CO₂ content, total base, chloride and total protein were made according to the methods already described.⁶

DISCUSSION

The results of all of the acid-base balance determinations are tabulated in the appendix (Table III) where individual variations for each case can be followed. Table II gives the results which were obtained when the various values were averaged according to the month of pregnancy. From these average values it can be seen that there is no general trend in the change of the acid-base balance concomitant with the progress of pregnancy. The changes which occur appear to have been established before the third month of pregnancy. A statistical analysis of the data is included in Table II.

The significant electrolyte changes which appear when a comparison of the average antepartum and postpartum values is made are: an increase of bicarbonate from 23.1 to 25.3; total protein from 14.4 to 15.6; total acid from 140.3 to 143.6; and total base from 147.1 to 150.0 m.Eq. The chloride concentration remains unchanged. These observations are in accord with those of previous workers shown in Table I, excepting those of Dieckmann and Wegner,⁴ where the changes are relatively small. Similar changes were also observed by Muntwyler, Limbach, Bill and Myers⁶ in a study of the acid-base balance changes in mild "toxemias" of pregnancy. In their work, however, the average chloride concentration was found to be 2.0 m.Eq. less in the postpartum samples (taken within two weeks following delivery) than in the antepartum samples.

The average antepartum and postpartum pH values (both colorimetric and electrometric) are comparatively constant and are slightly above the normal average of 7.4. Elsewhere we have stated¹¹ that "as a result of a large number of observations made on human plasma by the electrometric and colorimetric methods, we feel that the normal pH generally falls between 7.35 and 7.45, with an average of 7.4."

The distribution of the antepartum acid-base balance which represents 93 electrometric pH determinations on 44 normal pregnancies is shown in Fig. 1.

It will be observed that there is considerable scattering with six values (representing six cases) occurring above pH 7.45 and three values (representing three cases) occurring below 7.35. (It is only fair to note that 2 of the 44 cases, in which

TABLE II. INTERVAL AVERAGES OF THE ACID-BASE EQUILIBRIUM THROUGHOUT THE ANTEPARTUM AND POSTPARTUM PERIODS

INTERVAL	NO. DETN.	pH _e *	pH _c *	-HCO ₃ m.Eq.	-Cl m.Eq.	PROTEIN m.Eq.	TOTAL ACID m.Eq.	TOTAL BASE m.Eq.	UNDETN. ACID m.Eq.
<i>Antepartum:</i>									
8 mo.	4	7.42	7.47	22.7	101.1	14.0	137.8	142.7	4.9
6 and 7 mo.	23	7.39	7.39	23.3	102.2	14.4	139.8	145.5	5.7
4 and 5 mo.	26	7.41	7.425	23.2	103.5	14.5	141.2	148.1	6.9
2 and 3 mo.	28	7.41	7.42	23.7	102.8	14.3	140.3	145.7	5.4
1 mo.	23	7.41	7.40	23.3	101.7	14.7	139.7	147.0	7.3
2 days	9	7.42	7.445	22.1	104.0	14.9	141.0	146.1	5.1
In labor	13	7.395	7.41	22.1	102.7	14.9	139.7	149.1	9.4
<i>Postpartum:</i>									
3 days	11	7.41	7.40	24.7	103.5	14.7	142.9	150.2	7.3
7 days	21	7.41	7.40	25.0	102.2	16.1	143.3	149.7	6.4
1 mo.	19	7.41	7.40	25.3	101.9	15.5	142.7	150.6	7.9
2 to 7 mo.	14	7.41	7.41	26.6	102.6	15.8	145.0	149.0	4.0
Mean antepartum		7.411	7.426	23.1	102.8	14.4	140.3	147.1	6.8
Mean postpartum		7.416	7.403	25.3	102.6	15.6	143.6	150.0	6.4
Difference of means		0.005	0.0253	2.2	0.24	1.16	3.3	2.9	
Error of difference		0.0036	0.0055	0.172	0.319	0.169	0.357	0.485	
Ratio D/E		1.5	0.5	12.7	0.75	6.8	9.2	6.0	

*pH_e stands for electrometric pH and pH_c for colorimetric pH in this and Table III.

electrometric pH determinations were not made, showed high colorimetric pH values.) A similar distribution employing colorimetric pH values shows a somewhat greater scattering. In the series of 109 colorimetric determinations obtained upon the same 44 cases the pH value is greater than pH 7.45 in 21 instances (representing 16 cases), and below pH 7.35 in 11 instances (representing 9 cases). By employing a colorimetric correction of 0.30 pH to convert the colorimetric serum pH from 20° to 38° a comparison of 77 simultaneous colorimetric and electrometric determinations made upon the antepartum bloods of the above cases showed the colorimetric value to be within ± 0.02 pH, 33 times (43 per cent), and within ± 0.04 pH, 52 times (68 per cent). The agreement between the colorimetric and electrometric values in these cases is not as good as was obtained by us previously⁹ when plasma was employed. In the latter study 85 per cent of the plasma colorimetric pH values were within ± 0.04 pH of the correct value when a colorimetric

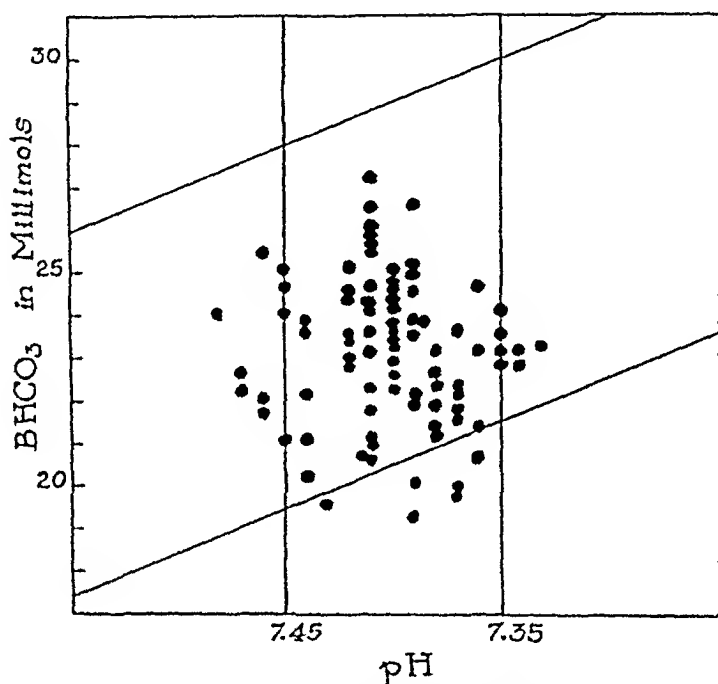


Fig. 1.—The distribution of the antepartum acid-base equilibrium in Van Slyke's graph. The pH boundaries have been narrowed to 7.45 to 7.35.

correction of 0.22 pH was employed. The reason for this difference in results is not apparent. One might infer that by the use of serum instead of plasma the colorimetric correction is less reliable. It was probably unfortunate that we did not use plasma in this study, since the colorimetric pH observations of Gaebler and Rosenet and Muntwyler, Limbach, Bill and Myers⁶ were carried out with plasma, but it was not realized that serum would require a different correction factor than plasma until the study was well under way, and the poorer agreement with the electrometric pH observations was not appreciated until the study was nearly completed.

In Fig. 1 it will be observed that the points tend to concentrate in the lower half of area 5 of Van Slyke's diagram.¹² This cannot be considered as more than a tendency toward a compensated alkali or CO_2 deficit.

TABLE III. ACID-BASE DETERMINATIONS DURING PREGNANCY

CASE	AGE	PARA	MO. OF PREG.*	pH _e	pH _c	CO ₂ m.Eq.	-Cl m.Eq.	BASE m.Eq.	PROTEIN m.Eq.
1	19	i	4	7.39	7.39	24.8	106.2	150.1	
			6	7.41	7.43	23.4	100.5	150.0	6.8
			8½	7.45	7.37	22.2	102.1	154.4	7.2
			9	7.41	7.46	22.1	98.2	146.9	7.3
			+ 1 wk.	7.43	7.40	26.0	102.0	150.5	6.6
			+ 1 mo.	7.45	7.44	25.7	103.1	157.3	6.5
2	19	i	3½	7.42	7.37	25.7	102.8	149.7	5.9
			6	7.42	7.44	26.3	103.1	153.3	5.2
			-10 hr.	7.44	7.38	21.3	104.5	152.0	5.6
			+ 1 mo.	7.44	7.38	28.5	101.5	160.0	6.5
3	16	i	4	7.40	7.36	25.0	104.5	148.8	5.7
			6	7.42	7.44	24.8	106.1	153.7	6.0
			8½	7.39	7.39	23.2	107.1	143.3	5.0
			+ 1 mo.	7.42	7.34	29.2	102.8	156.6	6.0
4	32	i	3½	7.38	7.36	23.1	102.9		5.0
			6		7.46	22.0	106.9	149.5	5.0
			9	7.47	7.47	23.5	105.5	157.7	5.3
			+ 1 wk.	7.40	7.44	24.8	104.0	153.9	6.1
			+ 1 mo.	7.46	7.47	24.7	105.6	146.2	6.1
5	24	vii	3	7.38	7.35	24.4	103.7	140.0	6.4
			7	7.35	7.36	24.5	103.6	148.3	6.5
			8½	7.34	7.34	24.4	104.8	151.1	6.6
			+ 1 mo.	7.42	7.33	27.4	102.2	153.3	6.5
6	34	ii	4½	7.44	7.46	25.8	103.5	146.7	5.6
			6	7.41	7.42	24.8	104.4	152.6	5.6
			9	7.36	7.37	26.0	103.1	150.3	5.8
			+ 1 wk.	7.38	7.40	29.2	98.8	149.6	6.1
			+ 1 mo.	7.41	7.38	28.1	104.4	155.0	5.6
7	26	i	3	7.43	7.42	20.5	106.0	148.8	5.3
			6	7.46	7.45	22.8	105.2	151.7	5.4
			8	7.44	7.42	24.4	104.2	157.5	5.3
			+ 1 wk.	7.41	7.45	24.9	103.0	144.4	6.1
			+ 1 mo.		7.37	25.3	105.1	143.7	5.6
8	19	i	3	7.39	7.33	21.1	103.1	144.2	5.5
			6	7.40	7.39	25.5	104.0	147.6	
			9	7.40	7.39	24.1	103.7	156.0	5.7
			+ 3 days	7.44	7.38	23.1	99.8	148.5	5.8
			+ 1 mo.	7.42	7.47	26.1	105.2	152.8	5.7
9	30	ii	4		7.36	23.4	103.1	144.1	6.3
			7		7.42	22.4	104.1	149.2	
			9		7.37	25.5	101.0	153.4	5.7
			+ 1 wk.	7.40	7.38	26.0	100.5	157.4	7.1
			+ 1 mo.			28.4	103.7	144.2	6.3
10	24	ii	4	7.41	7.42	22.9	105.4	149.0	
			7	7.39	7.44	23.2	103.6	146.4	6.3
			- 1 day			21.7	103.3	141.7	6.2
			+ 1 wk.	7.43	7.39	26.7	102.8	142.5	6.6
			+ 3 mo.	7.37	7.38	28.9	102.5	154.5	7.0

*Time immediately antepartum is indicated by a minus sign, and time postpartum by a plus.

TABLE III--CONT'D

CASE	AGE	PARA	MO. OF PRFG.*	PH _e	PH _v	CO ₂ mEq.	-Cl mEq.	BASE mEq.	PROTEIN mEq.
11	27	i	4		7.37	25.3	100.1	149.2	5.6
			6	7.41	7.38	21.7	102.2	151.0	6.3
			+ 2 days		7.43	22.7	107.2	141.0	
			+ 2 mo.	7.39	7.39	25.6	103.2	151.7	
12	18	i	4	7.36	7.39	24.5	102.5	149.2	5.4
			7	7.40	7.46	23.4	104.7	153.5	4.8
			8	7.41	7.40	22.7	100.1	147.9	4.9
			9	7.42	7.39	24.1	102.0	144.2	4.9
			+ 2 mo.	7.38	7.42	27.0	101.6	147.0	5.3
13	34	vi	2	7.39	7.48	24.6	102.6	143.5	4.5
			6	7.45	7.46	25.1	102.9	148.0	5.7
			7		7.37	22.9	100.9	138.9	
			8	7.42	7.45	24.2	103.5	145.5	5.4
			9	7.43	7.33	24.5	101.2	146.3	5.7
			+ 7 hr.			24.1	101.3	140.7	6.0
			+ 1 wk.	7.35	7.36	25.7	103.0	149.3	6.1
			+ 1 mo.	7.43	7.48	28.5	100.3	145.5	
14	23	i	6	7.36	7.44	21.8	103.0	151.7	7.1
			8	7.38	7.44	23.8	101.7	146.7	6.1
			9		7.34	22.3	102.7		
			+ 2 mo.	7.42	7.32	29.3	100.0	148.4	6.6
15	33	vi	4	7.39	7.44	22.6	106.4	146.4	5.6
			8	7.37	7.42	22.7	103.5	148.4	5.5
			9	7.46	7.49	23.1	100.3	142.7	5.7
			2 days	7.44	7.47	24.3	103.4	144.6	5.6
			1½ mo.		7.49	26.0	100.2	144.5	6.3
16	30	iv	5	7.35	7.39	24.1	101.7	146.9	5.2
			7	7.40	7.34	24.6	100.8	148.4	5.4
			8	7.38	7.37	25.1	103.1	144.0	5.7
			9	7.45	7.47	26.2	99.0	145.9	5.7
			+ 3 hr.	7.39		26.6	98.7	148.8	5.6
			+ 1 mo.	7.41	7.44	27.5	96.2	148.4	
17	19	iii	4	7.44	7.43	25.0	102.4	146.3	5.8
			7	7.41	7.40	25.5	99.5	145.6	5.2
			9		7.53	24.8	98.0	140.9	5.3
			+ 1 wk.	7.44	7.44	27.5	97.0	147.6	
			+ 7 mo.	7.43	7.48	28.4	101.0	153.8	7.4
18	20	i	5	7.40	7.38	24.5	99.8	140.4	5.8
			7		7.38	26.3	99.5	148.4	5.5
			9	7.46	7.50	26.6	104.0	140.3	5.1
			+ 2 mo.	7.41	7.38	28.3	99.3	141.5	4.7
19	21	i	4	7.39	7.39	26.4	99.0	142.9	5.9
			7	7.39	7.43	25.1	99.0	148.4	5.5
			8	7.48	7.50	25.1	100.6	143.8	5.6
			9			20.5	102.4	140.0	4.8
			+ 1 mo.	7.40	7.41	26.1	94.5	147.6	6.5
20	33	iv	5	7.33	7.40	24.7	104.7	144.0	5.3
			7	7.42	7.40	24.6	104.1	147.1	4.7
			8	7.47	7.53	23.3	103.1	146.3	4.5
			9		7.40	25.9	98.8	141.3	
			+ 2 mo.	7.41	7.44	27.6	109.1	151.0	5.4
21	25	ii	4		7.30	25.0	100.0	138.0	6.6
			7		7.33	26.5	101.9	156.1	5.5
			9		7.34	26.1	92.6	142.4	5.8
			+ 1 mo.	7.41	7.46	28.1	106.9	144.8	5.5

TABLE III—CONT'D

CASE	AGE	PARA	MO. OF PREG.*	pH _e	pH _c	CO ₂ m.Eq.	-Cl m.Eq.	BASE m.Eq.	PROTEIN m.Eq.
22	18	ii	2		7.46	23.8	102.2	146.2	4.9
			4	7.41	7.42	26.3	96.9	140.0	5.7
			7	7.39	7.38	27.0	102.4	141.5	5.7
			8	7.41	7.44	25.9	104.3	145.0	
			9	7.41	7.44	24.3	104.7	145.0	
			+ 2 mo.	7.40	7.44	27.8	101.0	153.0	6.1
23	16	i	3	7.41	7.43	26.8		144.8	
			7	7.41	7.45	26.9	109.2	146.5	
			- 7½ hr.	7.40		25.9	104.5	158.0	6.1
			+ 1 mo.	7.39	7.41	27.4	104.9	163.0	6.1
24	23	iii	6	7.41	7.45	25.4	100.8	142.2	5.3
			8	7.40	7.42	26.1	108.0	144.5	
			+ 6 days	7.40	7.45	27.0	105.7	153.1	5.0
			+ 3 mo.	7.38	7.38	29.2	102.4	160.5	5.3
25	23	i	5	7.40	7.55	25.6	98.8	141.6	5.6
			6	7.42	7.39	25.7	100.4	148.2	5.2
			9	7.39	7.46	25.1	100.9	152.0	6.1
			+ 1½ mo.	7.38	7.29	28.2	103.0	148.0	6.8
26	17	i	3	7.35		25.5	96.6	145.4	5.8
			6	7.40	7.44	26.3	107.0	144.0	5.5
			8	7.36	7.47	22.7	106.2	146.5	6.7
			- 9½ hr.	7.39		20.2	103.5	156.5	6.6
27	31	ii	- 8 hr.	7.35	7.25	25.0	101.5	148.0	5.3
			+ 4 days	7.42	7.30	29.9	98.2	149.4	5.5
			+ 1 wk.	7.39	7.40	25.7	100.3	146.3	6.1
28	21	i	- 3 days		7.36	23.9	98.2	141.1	5.6
			+ 4 days	7.32	7.30	23.2	100.2	143.2	5.4
29	20	i	- 6 hr.		7.33	23.4	93.5	142.2	5.2
			+ 1 wk.	7.39	7.31	24.3	106.0	142.5	6.0
30	21	i	- 7½ hr.		7.41	21.3	91.8	141.5	6.2
			+ 1 wk.	7.42	7.38	27.3	104.3	145.5	6.1
31	28	ii	-10 hr.	7.37	7.36	20.9	111.2	157.0	5.0
			+ 3 days	7.37	7.42	25.1	107.4	146.5	5.5
32	23	i	- 7 hr.	7.38	7.43	23.5	112.2	144.5	4.9
			+ 4 days	7.40	7.34	27.3	106.9	157.4	4.8
			+ 1 wk.			28.6	103.8	153.5	5.6
33	15	i	- 3 days	7.40	7.43	25.5	106.7	150.2	4.8
			+ 3 days		7.36	24.3	104.9	147.8	5.5
			+ 1 wk.	7.35	7.35	27.0	98.9	146.0	7.0
34	24	iii	- 2½ hr.	7.37	7.43	23.0	106.3	145.8	6.1
			+ 3 days		7.41	24.2	105.1	146.0	5.3
			+ 1 wk.		7.41	26.4	105.5	145.3	
35	20	i	-13 hr.	7.38	7.48	22.3	104.2	152.0	6.3
			+ 4 days	7.44	7.51	25.7	106.2	157.0	6.3
			+ 1 wk.	7.42	7.49	25.8	103.9	152.0	6.5
36	19	i	-12 hr.	7.43	7.55		102.2	145.2	7.0
			+ 1 wk.	7.41	7.42	26.4	101.9	153.0	7.4
37	22	iv	5 mo.	7.40	7.38	25.0	103.6	134.5	
			8	7.39	7.44	26.9	100.0	141.4	5.4
			+ 1 wk.		7.40	26.9	102.0	155.3	6.4
			+ 1 mo.	7.37	7.40	27.6	102.2	150.9	6.7

*Time immediately antepartum is indicated by a minus sign, and time postpartum by a plus.

TABLE III—CONT'D

CASE	AGE	PARA	MO. OF PREG.*	pH _a	pH _v	CO ₂ m.Eq.	-Cl m.Eq.	BASE m.Eq.	PROTEIN m.Eq.
38	21	i	2	7.41	7.43	22.1	102.0	139.1	6.8
			5	7.37	7.36	21.1	105.6	146.7	5.5
			8		7.40	21.2	101.8		
			+ 1 wk.		7.41	24.6	100.5	151.4	5.8
			+ 1 mo.	7.38	7.31	23.7	101.0	149.1	6.1
39	28	i	- 6 hr.	7.37	7.31	23.3	104.2	152.0	6.3
			+ 3 days	7.48	7.57	27.0	105.0	154.0	6.7
			+ 1 wk.	7.43	7.44	26.5	101.0	155.0	6.7
40	26	iii	4	7.42	7.41	24.0	101.3	147.4	5.7
			8	7.37	7.42	24.9	108.7	149.5	5.4
			9	7.37	7.41	23.3	105.4	153.8	5.6
			+ 2 mo.	7.41	7.49	28.8	106.2	150.2	6.7
41	22	i	5	7.40	7.41	25.6	101.4	144.4	5.6
			9	7.39	7.38	26.3	106.5	152.5	4.6
			+ 2 days	7.40	7.43	26.1	103.8	148.5	5.8
			+ 1 mo.	7.40	7.45	26.4	103.5	147.4	
42	22	i	2	7.41	7.54	26.0	97.5	142.2	5.7
			4	7.45	7.50	26.8	100.4	151.0	6.1
			7	7.41	7.45	26.4	103.7	140.0	6.1
			+ 2 wk.	7.44	7.46	28.8	101.0	160.2	6.0
43	19	ii	5	7.31	7.36	23.5	107.5	146.7	5.4
			6½	7.36	7.36	25.2	102.7	143.0	5.8
			8½		7.43	23.5	106.7	142.8	
			+ 1 mo.		7.35	26.0	96.7	148.8	6.1
44	24	i	-17 hr.	7.45	7.54	25.2	102.7	150.0	6.1
			+ 3 days	7.44	7.43	26.9	102.4		
			+ 1 wk.	7.45		27.3	101.0		6.8
45	22	i	3	7.41	7.42	27.5	102.3	143.5	5.4
			7		7.58	27.6	101.0	150.2	5.3
			9		7.23	23.9	96.2	148.8	6.1
			+ 2 mo.		7.47	27.6	106.6	146.5	
46	24	iv	5	7.42	7.40	25.3	102.5	139.5	5.5
			7	7.38	7.39	24.5	98.5	141.9	5.4
			9	7.40	7.45	24.0	100.2	144.0	5.6
			-11 hr.		7.43	19.5	102.6	142.7	7.0
			+ 3 days	7.40	7.46	27.9	98.8	152.0	7.0
			+ 2 mo.	7.42	7.44	30.0	101.3	145.3	7.3

Cases 1 to 37 inclusive were entirely normal; 38 and 39 showed only a slight albuminuria; and 40 to 44, inclusive, only blood pressure elevations to between 150 and 160, systolic. Cases 45 and 46 were severe toxemias and are not included in the calculations.

In their recent paper Dieckmann and Wegner⁴ state: "A study of the reports of pH in pregnancy seems to indicate that the change, if any, is toward the alkaline side. Kydd and his coworkers, . . ., stated that there is no change in pH. Myers and his coworkers, . . ., stated that the pH is definitely increased toward the alkaline side. . . . This controversy can be settled only by serial determinations of the carbon dioxide content and pH in at least twenty women who are studied at frequent intervals during pregnancy."

Although we have held the opinion that the pH was elevated in pregnancy, we have not intended to imply that this was always the case. In this connection we

stated:¹¹ "A high pH is not invariably found during pregnancy, for the apparent reason that the acid-base disturbance is compensated in many cases, but the evidence is quite conclusive that the pH is above the normal limits in a considerable number of cases."

Dieckmann and Wegner report all told 27 colorimetric pH observations. They state: "It is most unfortunate that more determinations of pH were not made in series A, because only serial observations can settle definitely the controversy as to whether the pH in pregnancy increases toward the alkaline side or shows no significant change. From repeated observations of pH since 1925, we believe that in normal pregnancy no significant changes occur, and furthermore, that it will require repeated determinations on the same patients throughout pregnancy to prove a change."

An inspection of their colorimetric pH data shows that, with the exception of one pH figure of 7.35, all their results were either 7.37 or 7.40. It is difficult to see how, even in strictly normal individuals, one would always obtain either one or the other of these two figures.

Doubtless Kydd, Oard and Peters,⁸ as well as Dieckmann and Wegner,⁴ will consider that our present electrometric pH observations are a vindication of their point of view that in normal pregnancy the pH of the blood remains unchanged. It is true that our observations covering the last six or seven months of pregnancy contain only a relatively small number of slightly elevated pH values (Fig. 1), but we still feel that the train of experimental data—increased volume of air respired, lowered CO₂ tension of the alveolar air, decreased blood bicarbonate and total base, all support the view that hyperventilation is the most important factor in the acid-base disturbance of pregnancy. This condition exists over such a long period of time that it would be only logical to expect compensation to occur, i.e., any elevation of the pH to return to normal. The fall in the blood bicarbonate in pregnancy can be due to a CO₂ deficit or an alkali deficit. The available experimental data support the former but not the latter view.

CONCLUSIONS

1. The slight changes of the acid-base balance of the blood which accompany normal pregnancy (principally a lowering of the bicarbonate and total base concentrations) become manifest before the third month of pregnancy.

2. Until a better explanation can be given, it is only logical to regard hyperventilation the most important factor in the decrease in blood bicarbonate observed throughout pregnancy.

3. The agreement between the colorimetric and electrometric pH values was not found to be as good when serum was employed as when plasma was used.

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THE TRANSVERSELY CONTRACTED MIDPELVIS WITH PARTICULAR REFERENCE TO FORCEPS DELIVERY

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IT HAS long been known that midforceps delivery in generally contracted and in funnel pelvis is attended by a high fetal mortality. The recent literature shows that difficult midforceps deliveries are still frequently encountered, and that the resulting fetal mortality is high.¹⁻³ The modern trend to broaden the indications for cesarean section has thus far accomplished little in reducing the number of unsuccessful midforceps deliveries; and it seems that a further increase in the incidence of abdominal delivery is not likely to yield better results, unless newer knowledge is brought to bear on the problem of the selection of cases for section.

A belief that such knowledge can be derived from a research based on more accurate pelvimetry, combined with a diligent study of the normal and pathologic mechanism of labor, prompted me to undertake an investigation of the subject, and has sustained my interest in the problem during the past seven years.

In a previous communication⁴ I submitted evidence to show that the narrow bispinous diameter is an important factor in the etiology of the persistent occipitoposterior position. The present study is an extension of the earlier work. Its main purpose is to determine the effect of a contraction in the width of the narrow pelvic plane on the course and mechanism of labor, particularly so far as midforceps delivery may be concerned.

The transverse diameter of the narrow pelvic plane has heretofore received only cursory attention. Interest has long been focused on the transverse diameter of the pelvic outlet. Recently⁵ attention has been directed to the transverse diameter of the pelvic inlet. But it is still assumed, without positive proof, that the width of the lower midpelvis is of little or no practical importance. Thoughtful consideration, however, shows that "the course of labor is most eventful at the level of the ischial spines, particularly in occipitoposterior positions.

It is here that the cardinal movements of internal rotation and descent must occur simultaneously, while flexion must be maintained or re-established."⁴ Furthermore, the greatest difficulties in midforceps delivery are usually encountered at this level of the pelvis, rather than at the pelvic outlet. The question of the clinical significance of the transversely contracted narrow pelvic plane deserves, therefore, more than the casual interest which it has thus far attracted.

METHODS AND MATERIALS

Material for the present study was obtained from 303 private cases, and from the last 3,638 deliveries at the San Joaquin General Hospital, a series of 3,941 consecutive cases; 1,290 of these were primiparas.

In the series of primiparas there were 67 midforceps deliveries, 2 versions, and 23 cesarean sections; 9 of the cesarean sections were done for disproportion in generally contracted and in funnel pelves. Among the multiparas, midforceps delivery was done in 4 cases, and version in 2 cases. Cesarean section was done in 27 cases, 3 of which were done for disproportion in justminor and in funnel pelves.

Version was done twice in the groups of generally contracted and funnel pelves, and both times after failure with forceps.

The low incidence of operative deliveries shows that a policy of conservatism was followed throughout, and that the series of cases is a truly representative one, unmodified, and uncomplicated by unnecessary artificial intervention.

The pelvic measurements in the entire series and all the operative deliveries were performed by me. Error due to the personal equation or to a misinterpretation of unfamiliar composite data was therefore entirely eliminated.

THE TRANSVERSE DIAMETERS OF THE NARROW PELVIC PLANE

1. *The Bispinous Diameter.*—The bispinous diameter was measured by means of an instrument devised in 1929.⁶ The average value for this diameter in 1,120 consecutive cases of the present series was found to be 10.48 cm. Bispinous diameters of 9.5 cm. or less were classed as contracted. Pelves with a narrow bispinous diameter were subdivided into two groups: (a) those with a minor contraction (9.5 cm. to 9.0 cm.), and (b) those with a major contraction (9.0 cm. or less). This classification is rather arbitrary, but it was found to be useful for practical purposes.

There were 207 cases with a narrow bispinous diameter among the primiparas, and 427 such cases among the multiparas, a total of 634 cases, or an incidence of 16.1 per cent. In 228 cases of the entire series the contraction of the bispinous diameter was of a major degree (an incidence of 5.8 per cent); in 32 of these cases the width of this diameter was 8.5 cm. to 8.0 cm., and in 6 cases 8.0 cm. or less.

2. *The Interischial Diameter.*—The bispinous diameter represents the width of only the posterior section of the narrow pelvic plane, since the spines are situated eccentrically, approximately 1 cm. posterior to the midpoint of the pelvis. In order to obtain the true transverse diameter, it is therefore necessary to supplement the measurement of the bispinous diameter with the measurement of a diameter nearer to the center of the pelves. The nearest approach to the diameter in question can be made by taking a measurement between the superior rami of the ischia, at points immediately anterior to the bases of the ischial spines. This new dimension of the pelvis will be designated as the "interischial diameter" (Fig. 1).

The interischial diameter can be readily measured as follows:

The bispinous diameter is first measured in the usual manner.⁶ After the measurement of this diameter the rings are carried directly anteriorly to the bases of the ischial spines, and a reading is taken while the rings are spread as far apart as the walls of the pelvis will permit.

At the beginning of the present study the width of the interischial diameter was determined only in selected cases; in the last 384 cases, it was measured routinely. The average value for this diameter was found to be 11.15 cm., with extreme variations of 8.0 cm. to 13.0 cm. As in the case of the bispinous diameter, the degree of contraction was designated as minor if the interischial diameter measured 10.0 cm. to 9.5 cm., and major if its width was 9.5 cm. or less.

The average difference between the interischial and bispinous diameters was 0.67 cm. This difference was 0.3 cm. or less in 19.5 per cent of the cases, and 1.0 cm. or more in 16.8 per cent of the cases. These data show, as one would expect, that the interischial diameter does not differ greatly from the bispinous diameter. Its measurement is, nevertheless, highly desirable if a true picture of the capacity of the lower midpelvis is to be obtained.

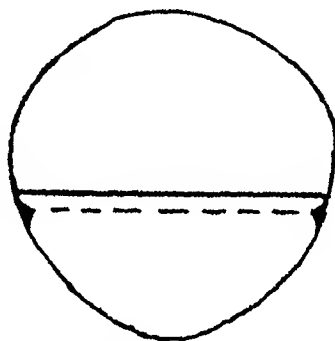


Fig. 1.—Outline of narrow pelvic plane. The upper solid line represents the interischial diameter.

In the sections to follow, reference will usually be made to the bispinous diameter for the reason that complete data are available on this diameter, and not because it is regarded as more representative than the interischial diameter. Pelves with a narrow bispinous or interischial diameter will often be referred to as pelves with a "transversely contracted narrow pelvic plane," or briefly as "transversely contracted pelves."

THE TRANSVERSE DIAMETER OF THE PELVIC OUTLET

The closely related transverse diameter of the outlet deserves special consideration in the present study. This diameter, commonly known as the biischial, will be referred to as the intertuberos diameter. The intertuberos diameter was measured by fitting a gauge between the ischial tuberosities, and adding 1.5 cm. to the reading obtained to compensate for the thickness of the skin and overlying fat, as recommended by DeLee. Measurements of the intertuberos diameter taken in this manner are 1.5 cm. greater than those obtained according to Williams' method. The average in the last 1,034 cases of the present series was found to be 10.87 cm. Pelves with an intertuberos diameter of 9.0 cm. or less (the equivalent of Williams' 7.5 cm.) were classed as pelves with a contracted outlet. There were 110 such cases in the entire series, an incidence of 2.8 per cent.

A close relationship was found between the intertuberos and interischial diameters. The average for these diameters, as just stated, was found to be

10.81 cm. and 11.15 cm., respectively. Unexpected differences were, however, frequently encountered. In as high as 32 per cent of the cases, the interischial diameter was narrower than the intertuberous diameter.

THE ANTEROPOSTERIOR DIAMETERS

In a study of the transverse diameters of the lower pelvis, it is necessary to take into consideration the anteroposterior diameters.

In the last 1,503 cases of the present series, the sacropubic or anteroposterior diameter of the narrow pelvic plane was measured by means of the internal outlet pelvimeter previously described.⁷ These measurements showed that the length of the sacropubic diameter varies between 8.8 cm. and 14.0 cm. (average 11.10 cm. in 1,070 consecutive cases). Diameters of 9.5 cm. or less were classed as contracted. There were 22 cases in the series, an incidence of 1.5 per cent. Among these, there was only one low forceps delivery in a case of justominor pelvis. In the remaining 21 cases of this series, delivery occurred spontaneously, and without difficulty; the average birth weight was 3,489 gm. This group of cases is, of course, small, but since the findings were uniformly negative it is permissible to conclude that serious dystocia due to an uncomplicated contraction of the sacropubic diameter must be very rare. This, however, does not exclude the possibility that a contracted sacropubic diameter may be a contributory cause of dystocia in pelvis in which the interischial diameter is narrow.

A plausible explanation for the above negative findings is to be seen in the fact that the sacropubic diameter is subject to considerable enlargement during delivery. In a series of 19 consecutive cases of spontaneous delivery in the usual dorsal position, it was found that the enlargement of the sacropubic diameter during delivery amounts to 0.7 cm. to 3.0 cm. (average 1.8 cm.). This enlargement occurs late in the second stage, at the time when the occiput stems under the pubic arch, and no longer recedes between pains. These measurements of the sacropubic diameter were made possible by marking the tip of the sacrum externally, so as to render its identification unmistakable during delivery.

The fact that the sacropubic diameter enlarges readily during spontaneous delivery shows that there is little to be gained from the commonly recommended exaggerated lithotomy position in cases of anteroposterior contraction of the outlet.

The posterior sagittal diameter of Klien was measured in the last 1,318 cases by means of the internal outlet pelvimeter.⁷ The average in 1,076 consecutive cases of this series was found to be 9.58 cm.

A close parallelism was found between the sacropubic and posterior sagittal diameters. The posterior sagittal is, of course, subject to enlargement during delivery in common with the sacropubic diameter. It may, therefore, be assumed that it is of less clinical significance than the constant and unyielding intertuberous diameter. The formulas in common use in which the posterior sagittal is raised to equal importance with the intertuberous diameter may consequently be very misleading.

THE TRANSVERSELY CONTRACTED MIDPELVIS AND THE PERSISTENT OCCIPITOPOSTERIOR POSITION IN PRIMIPARAS

In the group of 207 primiparas in whom the bispinous diameter was narrow there were 42 cases of the persistent occipitoposterior position; while in the series of 1,082 cases in which there was no contraction in this diameter there were only 17 such cases, an incidence of the persistent posterior position of 20.9 per cent and 1.6 per cent, respectively. These data support fully the conclusion previously reached, namely, that the narrow bispinous diameter is an important factor in the etiology of the persistent posterior position, and is thus indirectly an im-

portant cause of dystocia. This finding was recently confirmed by the direct roentgenologic observations of Caldwell and his coworkers.⁵ The association of the persistent posterior position with the transversely contracted narrow pelvic plane, and the resulting dystocia and obstructed labor, produce a clinical complex which may well be regarded as a syndrome.

THE TRANSVERSELY CONTRACTED MIDPELVIS AND MIDFORCEPS DELIVERY IN PRIMIPARAS

In the sections to follow, midforceps deliveries will be divided into two groups. The term "high midforceps delivery" will be applied to cases in which the lowest part of the head is 1 or 2 cm. below the level of the spines during a pain (station +1 or +2 according to DeLee's classification). Cases in which the station is +3 or +4 will be designated as "low midforceps deliveries." The term "low forceps delivery" will be restricted to cases in which the largest diameter of the head has passed the transverse diameter of the narrow pelvic plane (head on perineum or station 5).

Among the 1,290 primiparas of the present series there were, as already stated, 67 midforceps deliveries. The bispinous diameter was measured in 61 of these cases.

Among the 207 primiparas in whom the bispinous diameter was narrow there were 35 midforceps deliveries, an incidence of 16.6 per cent. In 15 of these cases the contraction of the bispinous diameter was of a major degree. Labor was complicated by the persistent posterior position, or by a transverse arrest, in 24 of the 35 cases (Tables I and II).

In the series of 1,082 primiparas in whom the bispinous diameter was not contracted there were 26 midforceps deliveries, an incidence of only 2.4 per cent. The persistent posterior position was encountered in only 8 cases of this group.

The incidence of midforceps delivery was thus 7 times greater in patients with a narrow bispinous diameter than in patients in whom there was no contraction of

TABLE I. MIDFORCEPS DELIVERY IN PELVES WITH A MINOR TRANSVERSE CONTRACTION OF THE NARROW PELVIC PLANE

CASE	INTER- TUB.	BISP.	SAC. PUB.	POSITION	STA- TION	WT.	RESISTANCE TO TRACTION
1	10.0	9.4		O.T.	1	4,145	Great
2	8.5	9.4		O.A.	2	4,080	Great
3	9.5	9.1	10.5	O.A.	2	4,110	Great
4	10.5	9.2	10.1	O.P.	2	3,068	Great
5	9.5	9.2		O.P.	2	4,080	Moderate
6	9.5	9.2	10.5	O.P.	2	4,695	Great
7	10.5	9.5		O.A.	4	3,360	Slight
8	10.0	9.5	9.5	O.P.	2	3,804	Moderate
9	8.5	9.5	10.0	O.P.	2	4,260	Moderate
10	10.5	9.4		O.P.	3	4,275	Slight
11	11.0	9.5		O.P.	4	4,050	Slight
12	8.5	9.2	11.5	M.A.	2	3,487	Great
13	8.5	9.3	11.5	O.P.	3	4,020	Slight
14	10.0	9.5	10.8	O.P.	3	3,720	Slight
15	10.5	9.5		O.A.	3	3,315	Slight
16	10.0	9.4	11.5	O.P.	4	4,002	Slight
17	10.5	9.2	11.2	O.P.	2	4,005	Slight
18	10.0	9.2	11.2	O.P.	3	3,990	Slight
19	10.5	9.5	11.0	O.P.	2	3,810	Slight
20	10.0	9.2	10.0	O.P.	4	4,335	Slight
21	11.0	9.1	9.5	O.P.	2	3,960	Great
Average	9.9	9.3	10.6			3,932	

this diameter. In addition to the high incidence of midforceps delivery in primiparas with a narrow bispinous diameter the difficulties in both instrumental rotation and traction were all limited to this group of cases.

TABLE II. MIDFORCEPS DELIVERY IN PELVES WITH A MAJOR TRANSVERSE CONTRACTION OF THE NARROW PELVIC PLANE

CASE	INTER-TUB.	BISP.	INTER-ISCH.	SAC. PUB.	POSITION	STATION	WT.	RESISTANCE TO TRACTION
1	10.0	9.0			O.P.	2	3,945	Moderate
2	10.0	8.6		9.8	O.P.	2	3,804	Great
3	9.5	8.8			O.P.	4	3,240	Slight
4	10.5	8.7		9.8	O.A.	4	4,350	Slight
5	8.5	9.0			O.A.	1	2,970	Great
6	10.0	9.0			O.P.	3	4,004	Great
7	9.0	9.0		9.3	O.A.	4	4,035	Slight
8	9.5	9.0			O.P.	4	3,540	Slight
9	9.5	8.0	8.9	9.2	O.A.	1	3,930	Great
10	9.5	8.6	9.5	9.5	O.P.	3	3,180	Great
11	8.5	8.5	9.0	10.8	O.A.	2	3,420	Great
12	10.5	9.0	9.0	10.3	O.P.	2	4,560	Great
13	10.0	8.5		11.0	O.P.	1	4,200	Great
14	9.5	9.0	9.1	11.2	O.P.	2	4,590	Great
15	9.5	9.0	10.0	11.4	O.A.	4	4,020	Slight
16	10.0	9.0		10.0	O.T.	2	4,080	Moderate
Average	9.7	8.8	9.3	10.2			3,867	

MINOR TRANSVERSE CONTRACTIONS AND MIDFORCEPS DELIVERY IN PRIMIPARAS

There were 21 midforceps deliveries in this group which consisted of 137 cases, an incidence of 15.3 per cent (Table I). Cases 7, 10, 11, 13, 14, 15, 16, 18, and 20 were low midforceps deliveries (Station 3 or 4). Labor was complicated by a persistent posterior position in 15 cases of this group; instrumental rotation was necessary in 5 of these (Cases 1, 4, 9, 11, and 21). Great resistance to both rotation and traction was encountered in all of these cases with the exception of Case 11. Very little obstruction to traction was, however, encountered in the 4 cases of occipitoanterior position of the series, and in the 12 cases of posterior position in which the malposition was corrected manually before the application of traction.

These data tend to show that obstruction to spontaneous and instrumental rotation is frequently encountered in cases of occipitoposterior position occurring in pelves with even a minor degree of transverse contraction in the narrow pelvic plane. There is, however, little resistance to traction in this type of pelvis, provided there is no malposition.

MAJOR TRANSVERSE CONTRACTIONS AND MIDFORCEPS DELIVERY

There were 75 primiparas in this group. Among these there were 16 midforceps deliveries, and 2 elective cesarean sections, an incidence of major operative intervention of 24.0 per cent (Table II). Eight of these instrumental deliveries, namely, Cases 1, 2, 5, 9, 11, 13, and 14, were high midforceps deliveries (Station 1 or 2). In Case 11 a pubiotomy was done after failure with forceps. Among the multiparas of this group there was only 1 major operation (Case 9).

Great and even insuperable resistance to forceps traction was encountered in 9 of the 16 cases in which instrumental delivery was attempted. Great resistance

to instrumental rotation was also met in 4 of the five cases in which this maneuver was attempted (Cases 1, 6, 10, and 12).

Spontaneous delivery, however, occurred in the remaining 57 cases of this series, with an average birth weight of 3,336 gm.

The series of cases in this subgroup is too small to justify final conclusions. Tentatively it is, however, permissible to assume that a transverse contraction of the narrow pelvic plane of a major degree is a serious obstacle to high midforceps delivery, even when the complicating factor of malpositions is entirely eliminated.

THE TRANSVERSELY CONTRACTED MIDPELVIS AND MIDFORCEPS DELIVERY IN MULTIPARAS

Among the 427 multiparas in whom the bispinous diameter was narrow there were 4 midforceps deliveries, an incidence of only 0.94 per cent, a strikingly lower incidence than in the series of primiparas (Tables I and II).

There were 28 cases of persistent occipitoposterior position in this group. In all of these, delivery occurred spontaneously, and in the majority of them without much difficulty.

RELATIVE IMPORTANCE OF TRANSVERSE CONTRACTIONS AT THE NARROW PELVIC PLANE, AND AT THE PELVIC OUTLET

The intertuberos diameter is of special interest in the present study since dystocia at lower levels of the pelvis has heretofore been generally attributed to contractions of this diameter,^{9, 10} while the transverse diameter of the narrow pelvic plane has been entirely overlooked as a possible cause of obstruction. A critical review of the subject shows, however, that the importance heretofore attached to the intertuberos diameter has been greatly overestimated. It is common knowledge that obstruction is rarely encountered in low forceps deliveries, and that the greatest resistance in midforceps deliveries, even in the so-called typical funnel pelvis, is usually met when the largest diameter of the head is at the level of the spines, and not when it is at the pelvic outlet. Furthermore, in justomino pelvis in which the bispinous diameter is narrow but in which there is a relatively slight contraction in the intertuberos diameter, the resistance to forceps traction is met at a level no higher than in funnel pelvis. Clinical experience, therefore, teaches that the transversely contracted narrow pelvic plane is the common denominator in justomino and in funnel pelvis, and that it is probably the chief cause of obstruction to instrumental rotation and traction in both of these types of pelvis.

This view is strongly supported by the following comparative clinical study of the intertuberos and bispinous diameters.

In the 634 cases of the present series in which the bispinous diameter was narrow, there were 95 cases in which there was an associated contraction of the outlet (an intertuberos diameter of 9.0 cm. or less). The average for the bispinous diameter in these cases was 8.80 cm. In this subgroup of 95 cases with a contracted outlet, there were 8 cases of obstructed labor, an incidence of 8.4 per cent. In the remaining 539 cases of the series in which the width of the outlet was within normal limits (9.5 cm. or over), there were 301 consecutive cases in which the bispinous diameter was of comparable width (average of 8.93 cm.). In this subgroup there were 23 cases of dystocia, an incidence of 7.6 per cent. The frequency of arrest of labor in these two groups is thus practically identical. It seems, therefore, that the incidence of dystocia is not appreciably increased in pelvis with a narrow bispinous diameter in which there is a coexistent contraction of the intertuberos diameter.

From these observations it follows that a contraction of the intertuberos diameter which is unassociated with a contraction in the bispinous diameter is

rarely a cause of serious dystocia, regardless of any ordinary degree of shortening in the posterior sagittal diameter. In other words, it seems that the real cause of dystocia and of obstruction to forceps delivery in pelves with a narrow intertuberos diameter is a coexistent contraction of the transverse diameter of the narrow pelvic plane, and not a contraction of the posterior sagittal diameter, as heretofore generally assumed. It may, therefore, be provisionally concluded that the transversely contracted narrow pelvic plane is a real obstacle in the cases under consideration, and is probably of far greater importance than the narrow intertuberos diameter as a cause of obstruction to forceps delivery, particularly to instrumental rotation.

THE INTERTUBEROUS AND INTERISCHIAL DIAMETERS AS A BASIS FOR THE CLASSIFICATION OF PELVES

Accurate measurements of the intertuberos and interischial diameters offer a basis for a simple and practical classification of transversely contracted pelves. Early in the course of the present study I gained the impression that pelves with a contracted outlet conform to the classical type of justominor rather than funnel pelvis, if the contraction of the intertuberos diameter is associated with a major contraction of the bispinous diameter. This impression has been strengthened by the results obtained from the recent measurements of the interischial diameter.

On the basis of these observations, transversely contracted pelves will be divided into three groups: "funnel pelves," "simple justominor pelves," and "flat justominor pelves." The term "funnel pelvis" will be applied to pelves with an intertuberos diameter of 9.0 cm. or less, provided that the width of the interischial diameter exceeds 10.0 cm. Pelves in which the interischial diameter measures 10.0 cm. or less will be designated as "simple justominor pelves," regardless of the width of the intertuberos diameter. Justominor pelves in which there is an associated contraction of the true conjugate will be referred to as "flat justominor pelves." The incidence of these types of pelvic contraction in the present series cannot be determined accurately, since measurements of the interischial diameter were taken only in a small number of the cases. For the present purpose, the interischial diameter may, however, be estimated by adding 0.7 cm. to the values obtained for the bispinous diameter. On this basis, the incidence of funnel and justominor pelves in the last 1,034 cases was 1.6 per cent and 5.8 per cent, respectively.

The following are good examples of the types of pelvic contraction under consideration:

Funnel Pelves: Cases 2, 9, 12, and 13 in Table I.

Simple Justominor Pelves: Cases 3, 4, 10, 11, 12, and 14 in Table II.

Flat Justominor Pelves: (Diagonal conjugate 11.5 cm. or less.) Cases 2, 9, and 13 in Table II.

This grouping of pelves may appear to be a step backward from the progress recently made by Caldwell and his associates in the classification of pelves.¹¹ There is, however, still a pressing need for a simple purely clinical classification of pelves which may be based on instrumental pelvimetry unaided by the x-ray. The present working classification is offered to fill this practical need.

COMMENT

It is a well-known fact that spontaneous uncomplicated delivery occurs in a large percentage of justominor and funnel pelves. The greatest difficulties are, however, frequently encountered in such cases

if instrumental delivery is attempted. Great resistance to instrumental rotation is frequently met in pelvis with even a minor degree of transverse contraction in the narrow pelvic plane. Serious obstruction to both rotation and traction is often encountered under circumstances where an arrest of labor is primarily due to inertia or to excessive soft tissue resistance, and not to actual disproportion. It seems, therefore, that disproportion in transversely contracted pelvis is seldom absolute or preexistent, but is usually due to the limitations of the present methods of forceps delivery, to an inefficiency of the force of instrumental rotation and traction as compared with the force of the natural powers of labor.

An analysis of the pathologic process involved leads one to suspect that deflexion is probably the abnormality in the mechanism of labor which is chiefly responsible for the obstruction to forceps delivery.

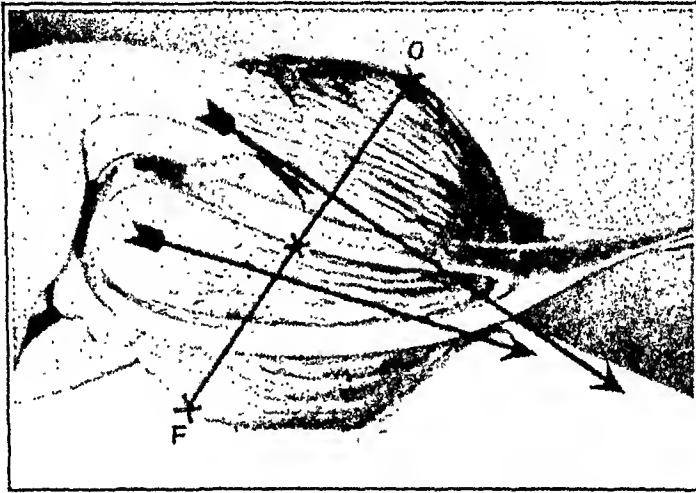


Fig. 2.—The direction of the forces of spontaneous and instrumental delivery. The upper arrow shows that the forces of natural labor are transmitted posterior to the ears, and at right angles to the occipitofrontal diameter (O.F.). The force of instrumental delivery, on the contrary, is applied chiefly anterior to the ears, and at an angle of approximately 110° to the occipitofrontal diameter. The result is a reversal of the occipitosincipital lever.

In spontaneous delivery this complication is of no serious consequence, since descent usually produces flexion, while flexion in turn favors descent. In instrumental delivery, however, there is a dissociation of these two cardinal movements: forceps traction causes descent but no flexion. In a recent communication¹² I pointed out that "this radical departure from the normal mechanism is due to the circumstance that forceps traction must necessarily be applied along the mentooccipital diameter (instead of the cervicovertical diameter along which the powers of labor are normally directed). The two-armed lever effect is therefore inevitably lost and the force of traction is distributed equally to the two poles of the head" (Fig. 2). The attempt commonly made of securing flexion by raising the handles of the forceps before compressing them is seldom rewarded with great success. The

failure is due to the circumstance that the head is often molded and is irreducibly fixed in an attitude of deflexion.

Serious obstruction is especially likely to result in transversely contracted pelves when labor is complicated by the occipitoposterior position, since deflexion is most marked in these cases, and is most persistent even after the malposition is corrected. Instrumental rotation under these circumstances, even with the Kielland forceps, is usually difficult and destructive; and if manual rotation fails, instrumental rotation and traction must be applied with the occiput in a position anywhere between 135° and 45° , and the enlarged anteroposterior diameter of the partially extended head must be forced through a contracted transverse diameter of the lower midpelvis. A diameter of the fetal head of 10.0 cm. or more (a dimension approaching in length that of the suboccipitofrontal diameter) is thus brought into relation with a narrow interischial diameter of 10.0 cm. or less. Poor flexion may thus be of little consequence in normal pelves, but in pelves with even a moderate contraction in the transverse diameter of the narrow pelvic plane, it may be a formidable complication, causing insuperable resistance to instrumental rotation, as well as great obstruction to forceps traction, even after malpositions are corrected, and after all the classical conditions for forceps are fulfilled. The disastrous results of midforceps delivery in cases of persistent posterior position are probably due not so much to the malposition per se, as to the accompanying deflexion, and the commonly associated transverse contraction of the narrow pelvic plane.

Engagement in the occipitoposterior position is therefore to be regarded as a danger signal in primiparas with a transversely contracted narrow pelvic plane, particularly so if the contraction is of a major degree. The outlook under such circumstances becomes increasingly unfavorable if rotation fails to occur as the end of the first stage of labor is approached.⁴ Serious difficulties are to be anticipated in such cases if the posterior position still persists after complete dilatation, and especially after rupture of the membranes.

The particularly unfavorable effect of deflexion in the cases under consideration would perhaps be minimized if the occiput could be rotated directly anteriorly, so as to bring the sagittal diameter of the head in direct relation with the relatively spacious anteroposterior diameter of the lower midpelvis. If this could be accomplished, the pelvic curve of the forceps would accurately conform to the curve of the pelvic axis, which would further facilitate traction. It is, however, unphysiologic, and it is often difficult or impossible to approach the direct anterior position any nearer than 45° , while the head is still in the midplane; in many of these cases direct anterior rotation becomes possible only after the head is well down on the perineum.

Midforceps delivery in transversely contracted pelvis may also be a contributory cause of disproportion in another important respect. The fenestrated blades commonly in use are flat from rim to rim; they have a width of about 4.5 cm., and a thickness of about 0.3 cm. At the lower midpelvis, which is nearly cylindrical in form, each blade may subtend an arc the width of which, including the thickness of the blade, would amount to approximately 1.0 cm. If the pelvic walls were firm and unyielding throughout, available midpelvic space would thus be reduced by 1.0 cm. on each side (Fig. 3). The actual reduction in the width of the midplane must, however, be less than this, since the bony framework of the lower midpelvis is interrupted posteriorly by the sacrospinous ligaments, and is padded anteriorly by the obturator internus. The only exposed bony segments encircling the narrow pelvic plane are the pubic rami, the ischial spines, and the tip of the sacrum. It is therefore unlikely that all four rims of the

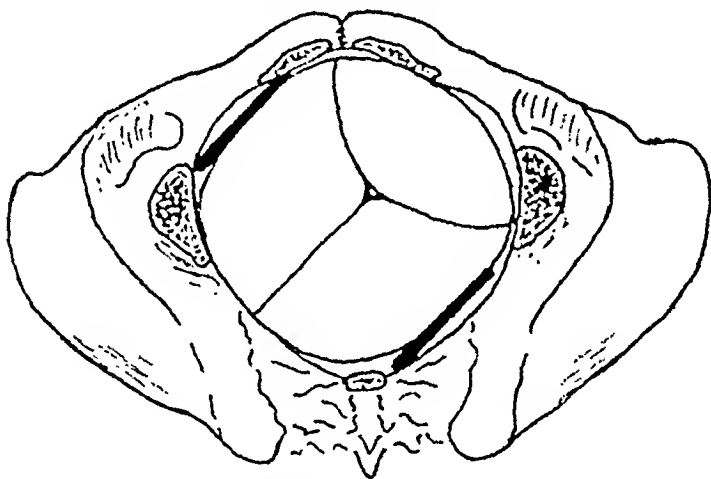


Fig. 3.—Diagram of a section at the narrow pelvic plane with a well-flexed head in position of O.L.A., and station + 4. The heavy straight lines at the sides of the head show the extent to which the forceps blades encroach on midpelvic space $\times 1\frac{1}{2}$. (Redrawn from DeLee's *Obstetrics*. W. B. Saunders Co.)

forceps blades may strike bony resistance on both sides of the pelvis at the same time. With due allowance for the buffer effect of the soft tissues, it is nevertheless highly probable that the forceps blades may encroach considerably on midpelvic space by "bridging over" the concave sides of the pelvis anterior to the spines (Fig. 3). In other words, when the presenting part is within the grasp of the forceps blades, it loses its freedom of adaptation to the hollow of the ischium which extends anteriorly above and below the level of the spines. The result is an inevitable shortening in the available width of the transverse diameter of the lower midpelvis.

PRACTICAL BEARING ON TREATMENT

The question of disproportion at the narrow pelvic plane is obviously a very complicated one. Factors other than spacial relations play a more important rôle here than at the pelvic inlet. Rigidity of

the soft parts, and weak or poorly coordinated uterine contractions, may be the cause of serious dystocia; and a malposition or a faulty attitude may offer insurmountable resistance to midforceps delivery, even in cases in which there is only minimal primary disproportion. Due to these variables the problem of disproportion at the narrow pelvic plane cannot be reduced to a simple formula in terms of centimeters or grams. Information gained from accurate measurements of the bispinous and interischial diameters may, nevertheless, be of great practical value.

A major contraction of the transverse diameter of the narrow pelvic plane may often be a factor of decisive importance in favor of cesarean section after a test of labor. In certain cases this degree of contraction may be an indication for elective cesarean section, as in elderly primiparas, and in multiparas in whom a previous instrumental delivery resulted disastrously. The indication for abdominal delivery may even be absolute in the rare cases of extreme contraction in which the width of the bispinous and interischial diameters falls below 7.75 cm., and 8.5 cm., respectively.

The present study has a particularly important bearing on various problems pertaining to the management of the persistent occipitoposterior position.

It is generally agreed that instrumental rotation, even with the Kielland forceps, is more difficult and more dangerous than manual rotation. The present analysis of the mechanism of labor shows that rotation by means of forceps is particularly destructive in transversely contracted pelvises. In this type of pelvis especially, an earnest effort should therefore be made to rotate the head manually; and if this fails, delivery in the direct occipitoposterior position may occasionally be attempted before restoring to the hazardous procedure of instrumental rotation. Cervical cesarean section may be fully justified under these circumstances even in the presence of only a minor degree of transverse contraction, if the head is at station 2 or higher, and if difficulty in manual rotation is to be anticipated, as in cases of tetany of the uterus, or contraction ring dystocia.

The views presented have also an important bearing on the question of treatment following manual rotation. It has long been taught that labor should be allowed to proceed spontaneously following the reduction of a posterior position provided, of course, that the malposition has been overcorrected, so that there is no tendency of the occiput to return to its original position. It has also been taught that forceps traction should be applied synchronously with the uterine contractions. The present study bears out the wisdom of these teachings. In selected cases in which the uterine contractions are powerful and well coordinated, even a brief period of labor following the correction of the malposition may bring about a remodeling and a fixation of the head in

an attitude approaching normal flexion. The flexion thus secured will be least disturbed during subsequent delivery if traction is applied only during uterine contractions.

As a general rule, it may be stated that in transversely contracted pelves the second stage of labor cannot be eliminated or curtailed without greatly increasing the difficulties and hazards of midforceps delivery. A policy of ultraconservatism is therefore clearly indicated in these cases, if delivery through the natural passages is decided upon. In the light of present knowledge "the early operative intervention" previously suggested⁴ should be limited to manual rotation; actual delivery may well be postponed until definite indications arise for the termination of labor.

To recapitulate, it may be stated that uncomplicated spontaneous delivery may be anticipated with greater confidence, and that the problem of midforceps delivery may be faced with less apprehension in the presence of a posterior position, and even in the presence of a considerable degree of outlet contraction, provided that the bispinous and interischial diameters are within normal limits. Conversely, even a minor degree of transverse contraction in the narrow pelvic plane may render the outlook for normal delivery decidedly unfavorable, if the head remains in the posterior position at station +2 or higher, for any length of time after the rupture of the membranes.

It is clear, therefore, that accurate and properly interpreted measurements of the bispinous and interischial diameters may yield knowledge of inestimable practical value; knowledge which may enable one to avoid some of the difficulties and hazards of instrumental delivery, and which may help to reduce materially the incidence of impossible midforceps deliveries, at the expense of only a slight and pardonable increase in the incidence of cesarean section.

The foregoing practical questions, and perhaps others, may come to mind. The magnitude and the importance of the subject forbid further consideration of these at the present time. Specific and final recommendations concerning treatment must be postponed, pending more extensive clinical observation and statistical study.

SUMMARY AND CONCLUSIONS

The clinical significance of the transverse diameter of the narrow pelvic plane, as represented by the bispinous diameter, was studied in a series of 3,941 consecutive cases; 1,290 of these were primiparas.

The observations made may be summarized as follows:

1. The transversely contracted narrow pelvic plane is associated with the persistent occipitoposterior position in a high percentage of cases. The constancy of this association, and the resulting dystocia, constitutes a clinical complex which may be regarded as a syndrome.

2. Operative intervention is necessary in a relatively large percentage of primiparas in whom there is a transverse contraction of the lower midpelvis. In 207 such cases of the present series there were 35 midforceps deliveries, an incidence of 16.6 per cent. In 1,082 cases in which the transverse diameter was not contracted there were 26 midforceps deliveries, an incidence of only 2.4 per cent.

3. Great resistance to instrumental rotation is frequently encountered in pelves with even a minor transverse contraction of the narrow pelvic plane (a bispinous diameter of 9.5 cm. to 9.0 cm.). In pelves with this degree of contraction, resistance to traction is, however, seldom met, provided there is no malposition.

4. Insurmountable resistance to forceps traction is often encountered in pelves with a major transverse contraction of the narrow pelvic plane (a bispinous diameter of 9.0 cm. or less), even after the correction of malpositions.

5. The resistance to rotation and traction in pelves with a transversely contracted narrow pelvic plane is probably in a large measure due to a persistence of deflexion incident to forceps traction, rather than to absolute or preexistent disproportion. Another probable cause of disproportion in these cases is an encroachment of the forceps blades on midpelvic space.

6. From the observations recorded, it is tentatively concluded that high midforceps delivery is usually contraindicated in pelves in which there is a major transverse contraction of the narrow pelvic plane, and that instrumental rotation is usually contraindicated even if the transverse contraction is only of a minor degree.

7. A new dimension of the pelvis, the interischial diameter, is described; and a new practical classification of transversely contracted pelves is presented.

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A CONTRIBUTION TO THE ETIOLOGY AND TREATMENT OF PUERPERAL INVERSION OF THE UTERUS*

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THERE is at the present time a very considerable difference of opinion as to the factors involved in the production of puerperal inversion of the uterus. The treatment of this unusual complication of labor is not well standardized, probably chiefly because of its rarity. The commonly accepted classification of puerperal inversion as acute, or chronic, is usually considered to be dependent solely upon the time elapsing after the occurrence of the inversion; namely, puerperal inversion discovered at any time less than a month after its occurrence has been termed acute, and cases noted more than one month after their origin, chronic. This classification is in many ways unsatisfactory. It is entirely arbitrary, bearing little if any relation to the pathology of the condition or the indicated treatment. Kellogg has recently suggested what seems to be a more rational classification, namely, acute, subacute, and chronic, depending not only upon the time elapsing after the occurrence of the inversion, but upon the pathology of the condition present. Puerperal inversion may be considered acute at any time before there is definite cervical contraction. Cervical contraction is usually well established after forty-eight hours. Cases are considered subacute where there is well-established cervical contraction and the case is of less than one month's duration. After one month, Kellogg accepts the usual classification and the case is considered chronic. This classification is more rational, not only because it is partly dependent upon the pathology found but also because it bears a very definite relation to the indicated treatment.

Five cases of puerperal inversion have been noted on the Obstetrical and Gynecological Services at Bellevue Hospital since 1924; these were reported by Barrows in 1934: since this time I have noted two additional cases.

A large group of writers believe that the principal etiologic factor is trauma, exerted usually in the form of improper Credé or traction on the cord. Huntington goes so far as to state that it is wise to consider puerperal inversion as usually the result of mismanagement on

*Read at a meeting of the New York Obstetrical Society, January 14, 1936.

the part of the obstetrician. It seems to me, however, that when one considers the number of parturient women attended by the unskilled, not only in the past but at present, and at the same time the extreme rarity of inversion, a necessary conclusion is that trauma and unskilled management of the third stage are only occasional etiologic factors. Küstner states that it is difficult to conceive of an inversion of the uterus being produced by pressure from above or traction on the cord if the uterus is firmly contracted. Crampton maintains that the cord will break before a firmly contracted uterus will invert. It seems necessary to have as etiologic factors not only a patent cervix but an abnormal degree of relaxation of the corpus. A true fundal



Fig. 1.—Gross photograph of section taken from the uterine fundus, showing many large organized blood sinuses.

implantation is the most unusual location for the placenta. A careful study of the literature as it relates to puerperal inversion shows that in almost every case in which the location of the placenta was noted, it was described as fundal. The rarity of fundal implantation corresponds to the infrequency of inversion. The importance of fundal implantation as an etiologic factor in inversion has been noted by many writers in the past (Bumm, Athill, McCullogh, Irving and others). The fact that inversion is more common in primigravidas may possibly be accounted for by the greater incidence of fundal implantation in the primigravida. In this series of seven cases the placental location was noted in but two instances and in both it was fundal.

CASE REPORT

The last case in this series was seen by me at the Victory Memorial Hospital, Brooklyn, in January, 1935. In this case a complete hysterectomy, abdominal, performed eight days after the occurrence of the inversion, permitted histologic study of the uterus. Blocks of tissue were removed from several areas, the exact fundus and three separate points in the corpus, below the fundus. There was no significant histologic variation in the three points below the fundus, hence but one characteristic area will be discussed. Microscopic slides of the entire thickness of the uterus were prepared from each of these areas (Figs. 1 and 2). Fig. 1 is from the fundal block, Fig. 2 from the lateral uterine wall block. Each of these slides was divided into three extremities for microscopic study, being designated as muscularis mucosa or endometrial, mid-zone, and serosal extremity. A study of the slide from the

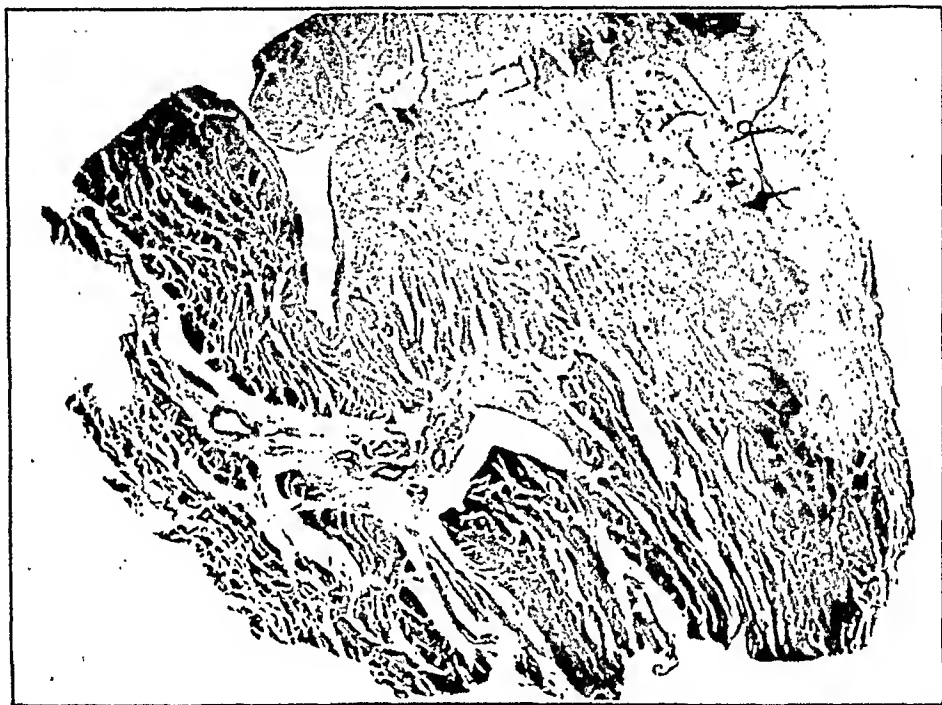


Fig. 2.—Gross photograph of section taken from the lateral uterine wall, showing lack of blood sinuses and comparatively little evidence of injury.

lateral uterine wall, muscularis mucosa or endometrial extremity. Fig. 3 shows a lack of large blood sinuses, edema of the muscle fibers but relatively little evidence of injury, no evidence of placental implantation. The lateral wall, mid-zone area, Fig. 4, shows edema of the myometrium and evidences of an inflammatory cell infiltration. The lateral wall, serosal extremity, Fig. 5, shows relatively little damage to the myometrium. There is some edema of the muscle fibers; the fibers are, however, intact. In contrast with this the microscopic findings in the section from the fundus are as follows: Fig. 6, from the mucosal area, shows many large blood sinuses undergoing organization, evidence of placental implantation. There is also marked edema of many muscle fibers. Fig. 7, from the mid-zone area, shows a large blood sinus extending to the myometrium, with organization of the sinus and destruction of the myometrium. Fig. 8 from the serosal extremity in the fundus shows edema with disintegration of the muscle fibers and an acute inflammatory cell infiltration. Fig. 9, a high power photomicrograph of the same section as Fig. 8, shows edema, polymorphonuclear invasion, with loss of nuclei in the muscle cells, and evidence of beginning necrosis.

Thus it is shown histologically that not only was the attachment of the placenta at the fundus in this case, but also that this attachment produced a definite destructive action upon the myometrium of the

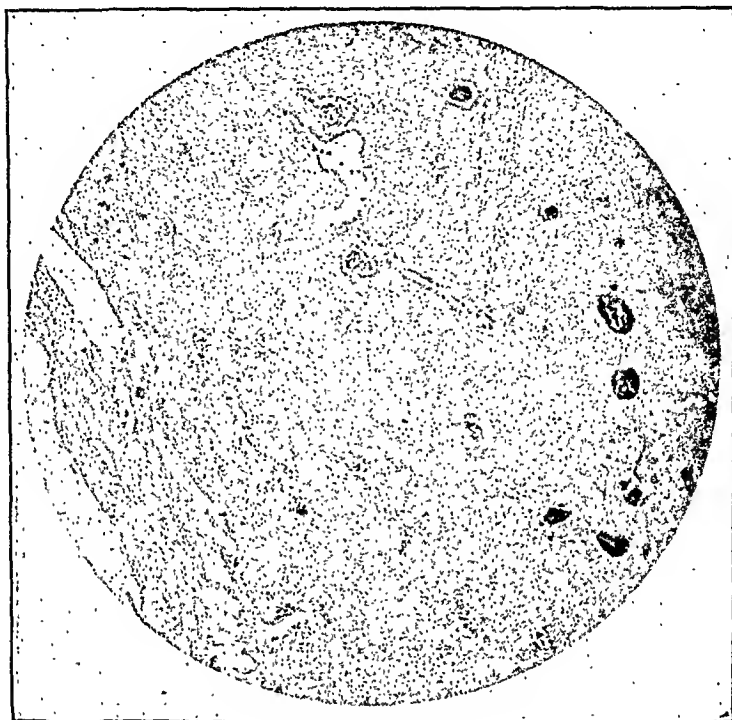


Fig. 3.—Photomicrograph of lateral uterine wall, muscularis-mucosa, showing a lack of large blood sinuses, edema of the muscle fibers but relatively little evidence of injury, no evidence of placental implantation.

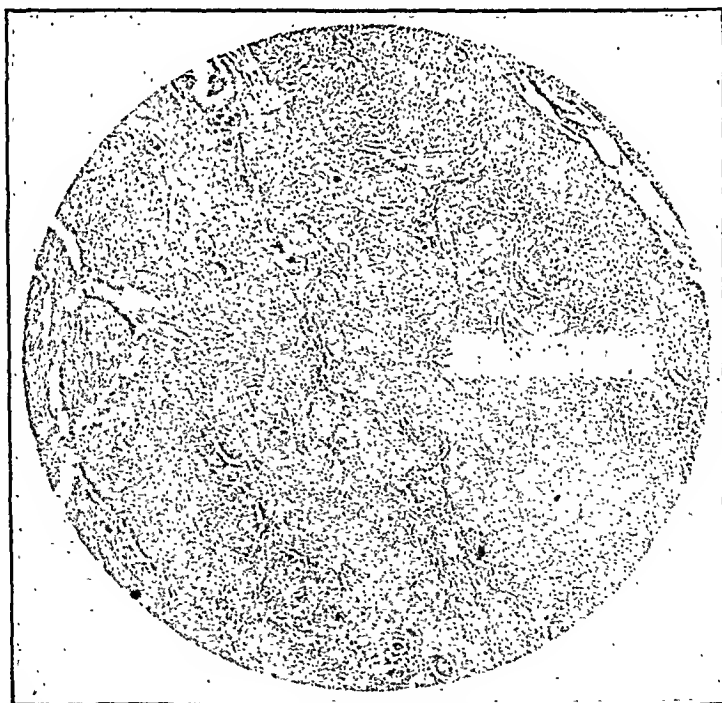


Fig. 4.—Photomicrograph of lateral uterine wall, mid-zone area, showing edema of myometrium, acute inflammatory cell infiltration.

fundus, thereby setting the stage, so to speak, for inversion. Observations at cesarean sections have shown that the placenta remains adherent to the uterus during the first few moments of retraction of the



Fig. 5.—Photomicrograph of lateral uterine wall, serosal extremity, showing but little damage to the myometrium. There is some edema of the muscle fibers; the fibers are, however, intact.

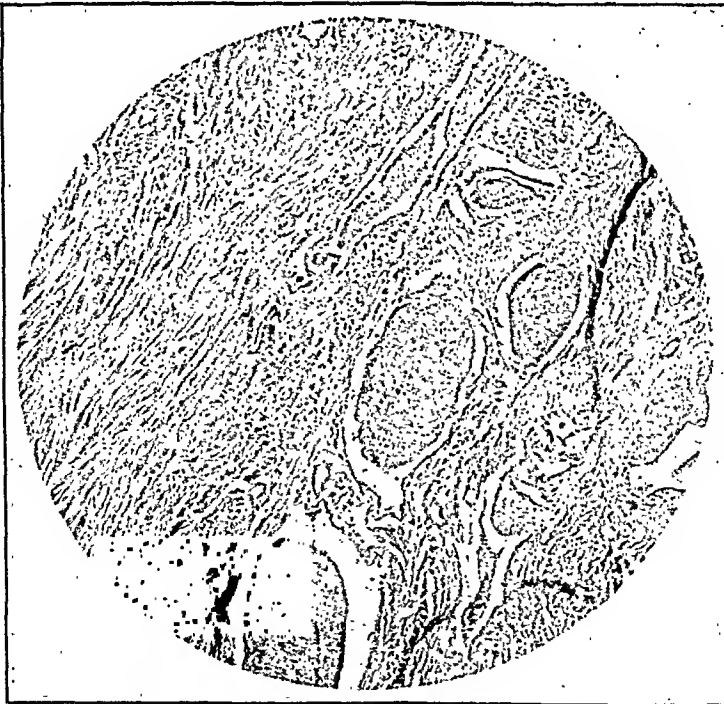


Fig. 6.—Photomicrograph of fundus uteri, muscularis-mucosa, showing large blood sinuses undergoing organization, evidence of placental implantation, edema of many muscle fibers.

myometrium. The uterine wall is thick everywhere except at the placental site. When the placental attachment is at the exact fundus we have, therefore, the mechanical factor of placental weight, the thin-

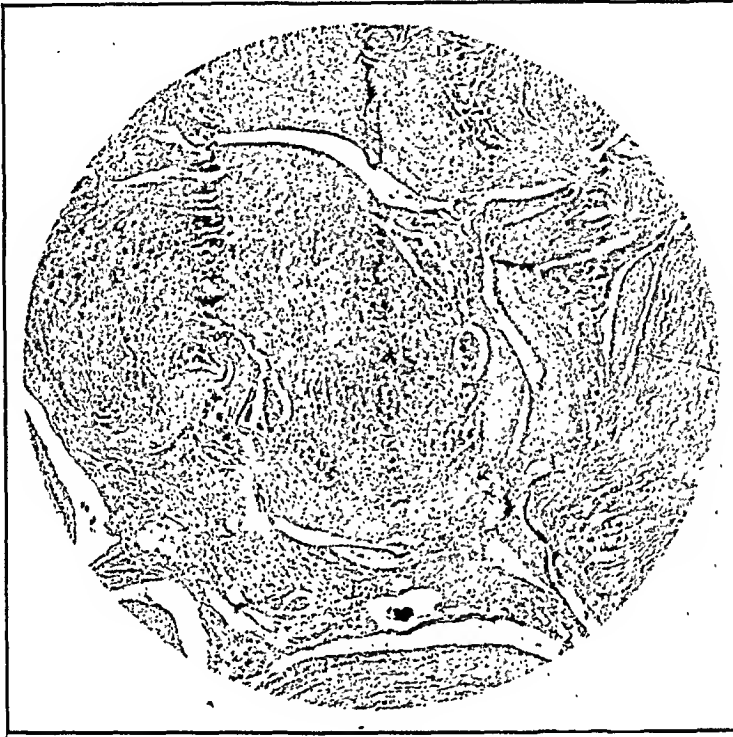


Fig. 7.—Photomicrograph of fundus uteri, mid-zone area, showing a large blood sinus extending to the myometrium with organization of the sinus and destruction of the myometrium.

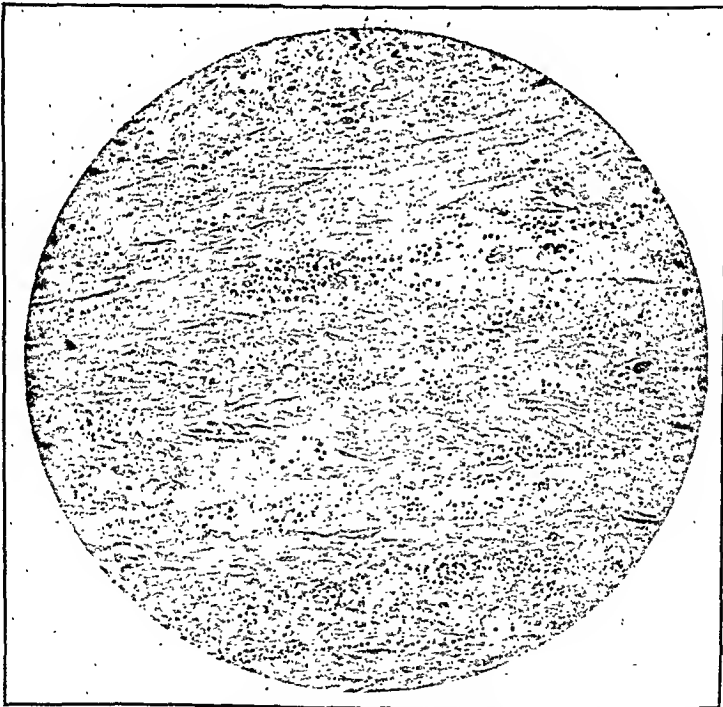


Fig. 8.—Photomicrograph of fundus uteri, serosal extremity, showing edema, disintegration of the muscle fibers and acute inflammatory cell infiltration.

ning of the myometrium at the placental site and the destructive effects of placentation, all exerting a definite influence in favor of inversion. Trauma either by traction from below or unskilled pressure from above may in some instances be a contributing factor but as capably stated by Reeve, "the accident may occur independent of anything done or omitted." Once a partial or incomplete inversion is produced the uterus may force the fundus out from above as it would a foreign body.

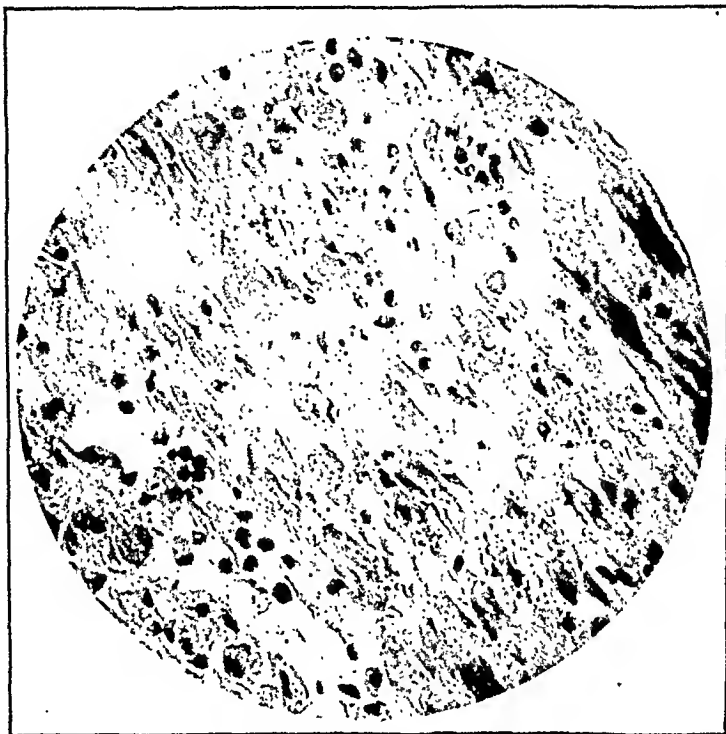


Fig. 9.—Same section as in Fig. 8. High power photomicrograph showing edema, polymorphonuclear invasion, loss of nuclei in muscle cells, evidence of beginning necrosis.

SUMMARY

The treatment of the seven cases comprising this series may be summarized as follows: There was one acute case, not in shock; this inversion was easily and successfully reduced by immediate manual reposition from below. There was one subacute case; the patient was operated upon successfully when ten days postpartum, after the technique of Spinelli. This patient died, following an easy labor, two years after her Spinelli operation. The cause of her death was rupture of the uterus, the rupture taking place through the scar of the Spinelli operation. There were five chronic cases. One reduced itself completely and spontaneously while the patient was in the hospital awaiting operation. In one a successful Spinelli operation was performed. Three of the patients with chronic cases were operated upon abdominally.

In one instance reduction was easily accomplished by manipulation alone. In a second laparotomy, the posterior uterine wall was incised in the manner suggested by Haultain. In the third laparotomy, a complete hysterectomy was done because of definite evidence of sepsis. There was no mortality in this series except in the one subacute case where death occurred two years after the Spinelli operation. This case illustrates a valid objection to the Spinelli operation in women of a child-bearing age.

Histologic evidence of fundal implantation of the placenta was found in a case of puerperal inversion, and its damaging influence upon the myometrium, in my belief, is an etiologic factor in inversion.

71 HALSEY STREET

A CONSIDERATION OF SOME OF THE ASPECTS OF STERILITY*

AN EVALUATION AFTER TEN YEARS

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TEN years ago I had the privilege of addressing this society on the same subject as tonight.¹ Now, as then, I can but touch upon a few points of the huge field of disturbed human fertility. I shall not discuss mechanical factors, as they are fairly well known today. I will stress mainly those points which to me appear to represent an advancement of our knowledge of the subject. In the past ten years some factors have become more important, others less so. Thus, the so-called obscure causes of sterility which I discussed in detail before, play less of a rôle today. "Relative sterility," or as I chose to call it, because it more nearly expresses actual conditions, "selective fertility," is no longer a mystery. Sperma immunity, differing blood groups in the two sex partners, psychic causes, have all been evaluated and found wanting. Vaginal acidity has been assayed and is not an adequate cause for otherwise unexplained sterility, especially since I was able to show that the introduction of the alkaline mucus from the Bartholinian glands on the male organ during coitus almost neutralizes any acidity present. The rôle of the cervix is also well understood today; it is a mechanical and not a chemical rôle. Blood and pus and bacteria have no effect on the sperms and I cannot corroborate the reports of Rosenthal² that *Bacillus coli* causes sperm agglutination. The varying solubility of cervical mucus in semen reported by Kurzrock and

*Presented at a meeting of the New York Obstetrical Society, March 10, 1936.

Miller³ I have shown⁴ to be dependent entirely on the stage of the menstrual cycle. With finer technique perhaps another test for the time of ovulation can be developed here. Varying uterine muscle irritability is likewise dependent on the stage of the menstrual cycle.

We thus arrive once again at what I stressed ten years ago, the importance of germ plasma defects, and I feel that it is along these lines that further advances of our knowledge must come. We must think beyond mechanical and simple chemical disturbances.

Seven years ago I had the temerity to propose an hypothesis based on local excessive ovarian hormone activity for the occurrence of adenomyosis and uterine fibromyomas.⁵ Since then Witherspoon and Butler,^{6, 7} Dean Lewis and Geschickter,⁸ have published similar theories. They gain support from the report of Papanicolaou that the epithelium of the endometrium is derived directly from the stroma and that endometrial epithelium, stroma, and uterine wall are all mesoderm. The relation of breast pathology to endocrine states is a further point of support. The objections voiced against this possible etiology of uterine fibromyomas so far seem to me not to be conclusive for reasons I cannot go into now. Furthermore, I do not bring up this subject in a controversial manner. I simply want to show that the very fact that such a theory can arise shows that we are getting away from the purely mechanistic way of thinking. Because carrying out the idea further leads to the inevitable sequential reasoning that abortions in cases of fibromyoma may be not simply mechanical but perhaps endocrine, and the same is true of abortions occurring in women with hypoplastic uteri. It has been said that succeeding pregnancies developed the uterus. Is it not more logical to go back to underlying principles and say sexual activity has stimulated the ovary or pituitary, or both, and thus the uterus gradually developed, while more important still, the ovary is enabled to produce normal ova? For only a normal ovum and a normal sperm can ever produce a normal zygote. Defects in either one of the two germ cells inevitably lead not only to sterility, but in the lesser degrees, to abortion, premature labors, stillbirths, and fetal anomalies. This should have been clear years ago. On the very surface it is evident that we have here an equally divided responsibility, but the difficulty of research in human beings and the incorrect dictum that it takes only one sperm to fertilize an ovum has probably led Cary,⁹ myself and others, who were near the truth years ago, astray. In addition, our superior male ego preferred to cast the blame on the woman and thus prevented us from seeing light and really understanding what is meant by the old adage "It takes two to make a baby." Thus today we talk less of the sterile man or woman, and more of the sterile couple, and examine both man and wife care-

fully and try to evaluate the combined factors found. Every investigation, of course, should begin with a careful anamnesis. This should determine, for reasons mentioned in previous papers, whether or not the man and wife were full-term babies. The time of puberty must be especially carefully evaluated, and the relation of the vitamins to the endocrines (Vogt,^{10, 11} Vogt-Møller,¹² Vogt-Møller and Bay¹³ and others) thought of. Menstruation, of course, is to be most carefully investigated. Even though we still do not know the actual reason for the menstrual bleeding, we do know that it is the waning of the corpus luteum and not the death of the ovum that causes the breaking up of the premenstrual endometrium. It is practically certain today that the ovum lives less than twenty-four hours, and can be fertilized for a still shorter time, partly perhaps because the ovum is an incomplete cell which contains only half the normal number of chromosomes, and partly because the ovum seems to acquire an albuminous envelope in the tube which makes sperm penetration impossible. The actual mechanism of the fertilization of the ovum today is known to be based very probably on differing electric charges, and the mystery of the prevention of polyspermism resolves itself into a neutralization of a difference of electrical potential. That the attraction of the ovum for the sperm is, however, not absolutely specific is shown by the penetration of a sperm head into a lymphocyte which I could observe under the microscope. Thereafter this lymphocyte had no more attraction for the other sperms. Another factor which must be considered is the today definitely established occurrence of anovulatory cyclic bleeding. It is interesting in this connection that Liegner¹⁴ has found that hypofunction of the pancreas causes atresia of the ovarian follicles and prevents corpus luteum formation. He has cured some cases of sterility in slender, underweight, nondiabetic women who ate well and sometimes had slight menstrual disturbances, by giving insulin. Some patients with amenorrhea have responded to the same treatment. I believe we can in some patients recognize two different types of bleeding clinically. One month breast changes will be prominent, dysmenorrhea practically absent, and the bleeding starts at the regular time in the usual way without further disturbance. A month or several months later, however, breast signs are practically absent, severe uterine cramps occur, and last for days before menstruation finally becomes established. At times slight bleeding for several days precedes the actual onset of the flow. In one such patient of mine endometrial biopsies showed a typical secretory endometrium in the first instance, and only a proliferative phase in the second type of bleeding.

As far as the absolute regularity of the menstrual cycle is concerned, it is, I believe, nonexistent. Many women think they really

are regular until the dates of the onset of menstrual bleeding are actually set down for six, or better, twelve months. Then variations of at least two to three days, and not infrequently of four to five days, will be seen. According to Knaus¹⁵ the onset of bleeding occurs fifteen days after ovulation. This seems a little too definite to me. We know that the size of the corpus luteum may vary, and thus it is perfectly logical to assume that its activity may last a day more or a day less at different times. In principle, however, I agree fully with Knaus. Finally it must be considered absolutely logical to assume that some ova produced even by a normal woman may be abnormal.

As far as the physical examination of the couple is concerned, I only want to stress here again that the size of the testis, unless atrophic, is no indicator of the fertility of the individual. Soft gonads, however, mean disturbed spermatogenesis, but unfortunately the converse is not true.

It is regrettable that there is no way of determining germ plasma defects in the female except by indirect methods. In the male we are more fortunate, and I feel that the detailed semen examination described by me ten years ago has done much to explain many otherwise obscure cases of sterility and definitely proved the rôle of the male in abortions, stillbirths, and fetal anomalies. I feel that the evaluation of seminal cytology (and the biometrical studies must not be neglected) will become increasingly important as more physicians make use of the method. At any rate, this detailed semen examination has done away with the totally erroneous conception that fertilizing power and motility of the spermatozoa are synonymous. Fertilizing power is undoubtedly lost long before motility ceases, and sperms which never were normal and evidently are totally incapable of fertilizing an ovum may be very actively motile. Nevertheless, motility of the sperms in animals with internal fertilization of the ovum is a *sine qua non* of pregnancy, and the evaluation of motility in any semen specimen is an extremely difficult problem. If the motility in a specimen is good we know where we stand, but if it is not good, we must be extremely careful in making a diagnosis. I have had specimens from normally fertile men where all the sperms were dead after only five minutes in a condom. Again in a normally fertile couple I have taken semen from the vault of the vagina and cervix one hour after intercourse and found practically only dead sperms. I have examined a semen specimen forty-five minutes old in which the first drop showed no motile sperms, whereas all the other drops examined thereafter showed perfectly normal conditions. The evaluation of sperm motility to me represents a great problem. There are here so many imponderables that constant vigilance is necessary to avoid serious misinterpretations.

As far as the, at one time so much talked of, sniffing sperm cell is concerned, we know today that it is nothing more than a temporarily or permanently slowed down cell, and we also know that the sperm head does not expand and contract, although this illusion may be produced by optic refraction.

As far as the number of the sperms is concerned, moderate oligospermia is compatible with normal fertility. One must, however, distinguish between oligospermia with a normal morphology and one with an abnormal seminal picture. A disregard of this fact makes most of the reports in the literature on oligospermia valueless.

As about motility I must also say a word of warning about the detailed semen examination described by me ten years ago. Even the most detailed examination will fail unless we are in a position to weigh every particle of evidence presented, and for the same reason, experience is necessary to evaluate properly seminal cytology and biometrics.

I continually get requests for my technic, because some one wants to try out the method on some case, or some physician wants his nurse or secretary to carry out the examinations. These same men would never dream of diagnosing a cervical biopsy, or intrusting this to their nurse or secretary, yet they fail utterly to realize that the evaluation of the seminal picture is just as much a question of morphology as diagnosing an early carcinoma of the cervix. Many times the treatment, even a laparotomy of the wife, depends on the result of the semen examination. In fact, unless the investigator is a trained pathologist, he will not be able to utilize to its fullest extent the seminal morphology and biometrics presented by each case. And it is significant that the only man who asked me "How long will it take me to learn what I am looking at?" was a pathologist. It is true, in general, that certain percentages of abnormal sperm heads can be used to predicate disturbed fertility and still higher ones sterility. At the same time a simple mechanical summation of the findings is not sufficient. The years have shown me that the percentages I set up some years ago¹⁶⁻¹⁸ roughly hold good; that is, patients with less than 20 per cent abnormal sperm heads and a coefficient of variability of less than 11 may be considered normal. With a sperm count showing 20 to 25 per cent of abnormal heads and a coefficient of variability around 11.5, disturbed spermatogenesis is to be assumed. Above that clinical sterility usually prevails. However, in human beings, where intercourse is repeated again and again, it stands to reason that even couples with a relatively low degree of fertility may finally achieve offspring.

However, as I said before, these are but the general facts; counts even below 20 per cent abnormal sperm heads may denote sterility, if

narrow and tapering heads or sickle-shaped heads are marked and total 8 to 10 per cent or more. Again, a rather high total count, but with many round heads, is better than the total head count would imply, since my experience over the years has shown that round sperm heads are not very important. Also two head counts with exactly the same total number of abnormal sperm heads and even the same percentages of each type of sperm head abnormality are not necessarily to be regarded as identical. Tapering and narrow and sickle-shaped heads are perhaps the most sinister types of sperm head changes, yet in one specimen the cells, though tapering and narrow, may be much less so than in another where very long and very narrow heads are seen, which indicates a much more intense spermatogenic disturbance. In the same way a slightly narrow sperm head in a specimen in which most of the heads are well rounded is to be evaluated differently than the same type of sperm head in a specimen with less rounded sperm heads. The same of course applies to small and large heads. Thus a semen may show decided improvement, even though the total abnormal sperm count remains the same.

I am often asked if double sperm forms have any connection with twin births. This is to be denied absolutely. Double sperm forms are abnormal sperms, but even if they were normal, remembering thigmotaxis, it would be impossible to visualize how such a double sperm form would penetrate the ovum with both its heads.

Although the results of my semen investigations have been confirmed by most authors, some objections have been voiced. It was claimed that the seminal morphology was subject to change. Since the constancy of the seminal picture is the first requisite for the value of this type of examination, this point naturally was originally investigated by me. I can say definitely that the seminal picture will change with increasing age or disease, but will not change suddenly without easily traceable, adequate cause. Otherwise occurring sudden morphologic changes are due either to mistakes or deliberate deception. My staining technic was also objected to, and it was claimed that cell abnormalities were artificially produced by it. Naturally this possibility occurred to me from the very first and was thoroughly tested out by me and rechecked since then. In no case did the count or the biometries show changes beyond the probability of error. I can say further that I have yet to see stained seminal smears which can compare in clearness and detail with my properly prepared slides. One must, however, avoid errors of technic.

Another objection which was made was that the sperm counts did not allow judging of the fertility. Here, however, the evaluation was often based on those couples with children and those without children. That this is not a proper classification has been pointed out before by

me in discussing the breeding record. Again if one counts all minor variations of the sperm heads which should still be regarded as normal one can easily obtain entirely erroneous results.

Finally it was objected that a difference of 5 per cent or more of abnormal sperm heads should make no difference. However, 5 of 20 (normal limit) is 25 per cent, and 25 per cent variation in thyroid function, for example, may in itself alone produce sterility. Aside from this, as pointed out before, the abnormal sperm heads are but an indication of the degree of spermatogenic disturbance, and mean, if of sufficient intensity, that all the other cells would be incapable of fertilizing the ovum, even though they looked normal.

Aside from morphologic and biometric facts regarding the spermatozoa, the ten years that have passed have also increased our knowledge of spermatogenesis. We know today that the seminal vesicles are not the reservoirs for the spermatozoa, but their graveyard, and that the sperms produced in the testis and endowed with some motility move on to the tail of the epididymis, maturing as they go. In the tail of the epididymis the sperms are stored, kept immotile by lack of oxygen and inhibiting secretions of the epithelium of that region. We have learned that the scrotum has a definite temperature-regulating function, and that its temperature in man is 2.7° to 7.8° C. below body temperature. I wish I had time to go into these interesting questions in detail, but I can only give you the conclusions drawn from the reports of many authors and from my own work, and that is that normal body temperature kills all sperms in a short time. At the very most they do not live longer than forty-eight hours, and personally I have found that they die in twenty-four hours. However, this is only judged by motility and this, as previously stated, has nothing to do with fertilizing power.

If now we gather up the threads spun so far we find that the human female has no definite estrus, ovulates but once a month, produces an ovum which lives at most a day, and kills off the spermatozoa in her genital tract in forty-eight hours or less. We thus come to the inevitable conclusion that conception in a woman is possible for only a few days of the whole menstrual cycle and that pregnancy is much more of a hit and miss affair than in many animals, especially those with a definite estrus. There is a vast amount of evidence today to support such a conclusion. I myself have now observed four normally fertile, carefully examined, couples from nine to three years who used no contraceptives at first during the week before menstruation, and for several years now for the periods from the end of menstruation to within four days of the calculated time of ovulation and for the last twelve days preceding menstruation. The net result of over 1,200 performed sexual acts during these periods of the men-

strual interval was one extremely doubtful abortion. This woman passed some rather large clots. There was no other evidence of pregnancy. The work of Knans¹⁵ and Ogino^{19, 20} is even more conclusive, and Hartman's²¹ investigations on monkeys carry additional weight.

It is true that there have been objections voiced to such periodic fertility in the human female. It is claimed by some that a woman may conceive at any time of the menstrual cycle and the finding of living sperm in the female genital tract has been reported fourteen, twenty, and even forty days after the last alleged intercourse. However, the only fact these authors proved so far is their own childlike faith in the statements of unconscions or vicious prevaricators. The memory for exact dates is always notoriously and thoroughly inaccurate, so that only written data that really seem to have been made at the time stated should be accepted.

Considering then the practically physiologic barriers to conception in the human female and our imperfect knowledge of the ductless glands, it is small wonder that many disturbances of fertility, based as they may be, on congenital or acquired defects or imbalances, should be far beyond our humble powers of analysis and therapy.

This being a gynecological society it hardly behooves me to discuss here the therapy of the female. May I be permitted, however, to say a few words about the treatment of the male with spermatogenetic disturbance? May I stress again the close relation of general physical health to fertility and the importance of a feasible reduction in the frequency of sexual congress? I want to add also that all forms of therapy begin by having a basal metabolism determination (and the same applies to my women patients). It seems significant to me that practically every single man with disturbed spermatogenesis has had a basal metabolism at least somewhat below normal. I feel that even slightly lowered thyroid function should be corrected, and have the impression that the amount of good which can be accomplished by thyroid therapy is not expressed entirely by the figure obtained by the basal metabolism test.

Aside from the thyroid, other endocrine therapy has been disappointing in many hands. The anterior pituitary-like hormone from the urine is a luteinizing hormone, and though it affects the interstitial testicular cells, as I have proved to my own satisfaction, it has no action on spermatogenesis, despite numerous reports in the literature to the contrary. Attempts to achieve pituitary stimulation with small doses of x-rays have also proved disappointing in the few cases on which I tried it.

Through the courtesy of Parke Davis and Co., I now have a gonadotropic hormone made directly from the anterior pituitary which has

shown very promising results in some cases. I have, however, at present not enough experience to go beyond this statement. Vitamin E, which seems necessary to growing cells, and thus would be necessary in the male in whom the spermatozoa are constantly being produced, and in the pregnant woman, less so in the nonpregnant female, I also use and apparently with good results. In another ten years perhaps we may know something about the therapy indicated in each case. Under all circumstances, however, the chief requisite is individualization. I feel that too much one-sided concentration on the endocrines, the vitamins, x-ray stimulation, obliteration of mechanical effects, and too great efforts to achieve pregnancy in a childless couple under any conditions have prevented us from perceiving the main problem, which is not how can we get a childless woman to conceive, but how must we treat a clinically sterile couple so that they can have a *normal* child? Before any form of therapy is instituted let us know, as far as this is humanly possible, that germ plasm abnormalities do not exist. Let us at least, in the simple way I have described, make sure of the male. Ten years ago I asked the question whether it were even worth while in many cases to try to save products of gestation that nature was trying to get rid of. In the last ten years my own experience has given me the categorical answer that it is not. It may perhaps shock some of you here tonight when I say that unless both parents have been carefully examined, I make no special efforts to try to save these very often abnormal products of gestation. Only when I know, as far as this is possible, that the husband is normal do I essay special therapy in the wife. Perhaps some products of gestation which might be saved by strenuous efforts are lost in this way, but the disappointment of a pregnancy ending in abortion is as nothing compared to the agony of the parents whose fondest hopes for a healthy and happy baby have been blasted by the birth of some misbegotten human caricature whose very being often turns love to dust and ashes, and whose continued existence is a constant source of anguish, compared to which the purely physical torture of a Tantalus is but a childish prank.

As physicians it is our duty to alleviate suffering. Let us not through thoughtlessness or neglect increase it. Let us get away from looking at infertility as a purely mechanical or chemical problem; let us concentrate our efforts on trying to determine the quality of the germ plasm of both sex partners. As our knowledge increases we will be able to do more and more in such cases of germ plasm abnormalities, and inevitably stages of improvement will thus be reached where conception is possible, but not yet the production of a normal child. As leaders of your profession, it is up to you then not to try under all circumstances to have a woman conceive, but even to prevent the

possibility of pregnancy unless you feel that normal offspring are at least probable. Unfortunately we will never be able to prevent all abnormalities, but with our imperfect knowledge, such as it is, let us do the best we can.

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30 EAST FIFTY-EIGHTH STREET

A STATISTICAL SURVEY OF ECLAMPSIA*

BASED ON SIX YEARS' EXPERIENCE IN PHILADELPHIA LYING-IN HOSPITAL

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THIS paper presents no new theories of etiology or treatment of eclampsia, and no new recommendations, but consists entirely of a statistical summary of our experience with this condition at the Philadelphia Lying-In Hospital from July 1, 1929 to July 1, 1935. The survey includes 12,601 patients, 38.1 per cent of whom were primigravidas and 61.9 per cent multiparas. There were 43 eclamptic patients in this group, of which 40 were ward and 3 were private patients. The inci-

TABLE I. TOTAL INCIDENCE

	RATIO	PER CENT
Our Series	1 in 293.0	0.34
Collected (Stander)	1 in 253.7	0.39

dence of eclampsia was 1 in 293 or 0.34 per cent. Hinselmann concluded from a study of statistics published up to 1924 that eclampsia occurs once in every 253.7 women entering a lying-in hospital (0.39 per cent). Thus the incidence in our series does not differ greatly from that in lying-in hospitals the world over.

*Read before the Obstetrical Society of Philadelphia, March 5, 1936.

INCIDENCE IN REFERENCE TO SEASON

As early as 1825 Smellie attributed a certain influence to atmospheric conditions; Olshausen, in 1890, stated that eclampsia varies with the seasons; Croom, from a study of the material of the Edinburgh Maternity Hospital, concluded that a sudden alteration in the temperature and rainfall, irrespective of any particular season, favors the development of eclampsia. Harrar found that the highest fre-

TABLE II. INCIDENCE RE SEASON

SPRING	SUMMER	AUTUMN	WINTER
21%	21%	35%	23%

quency was during the month of April, and that unsettled, damp, and cold weather is accompanied by an increased incidence of eclampsia. In our series there is no striking seasonal variation: 21 per cent occurred in the spring; 21 per cent in the summer; 35 per cent in the fall; and 23 per cent in the winter.

INCIDENCE IN REFERENCE TO PARITY

As early as 1768, Denman observed that primigravidas were more frequently affected than multiparas. Statistical studies indicate that eclampsia occurs about 8 times more frequently among primigravidas. In our series there were 31 eclampsias among 4,802 primigravidas (1 in 155 or 0.645 per cent), while in 7,799 multiparas only 12 patients developed eclampsia (1 in 650 or 0.154 per cent). Thus, in our group eclampsia occurred approximately 4 times as frequently among primigravidous

TABLE III. INCIDENCE RE PARITY

	TOTAL NUMBER	NUMBER OF ECLAMPTICS	PER CENT ECLAMPTICS
Primigravidas	4,802	31 (1 in 155)	0.645
Multiparas	7,799	12 (1 in 650)	0.154

patients. The 7 per cent incidence of twin pregnancies is in accord with numerous previous observations.

INCIDENCE WITH REFERENCE TO AGE

The youngest patient in this series was fifteen and the oldest was forty-three. The distribution by decades was as follows: second decade, 39.5 per cent; third, 41.9 per cent; fourth, 9.3 per cent; and fifth, 9.3 per cent. More than four-fifths of the patients were under the age of thirty years.

TIME IN PREGNANCY

The average duration of pregnancy at which eclampsia developed was 36.4 weeks. The earliest case was at the twenty-eighth week and the latest occurred in a patient who, according to her own statement, was four weeks past term.

INCIDENCE IN REFERENCE TO LABOR

Eclampsia occurred before the onset of labor in 65 per cent of our cases, during labor in 9 per cent, and after labor in 25 per cent. These figures are somewhat at variance with collected statistics in which the incidence is as follows: antepartum, 26 per cent; intrapartum, 53 per cent; and postpartum, 21 per cent.

TABLE IV. INCIDENCE RE LABOR

	ANTEPARTUM PER CENT	INTRAPARTUM PER CENT	POSTPARTUM PER CENT
Our Series	65	9	25
Collected (Stander)	26	53	21

INFLUENCE OF PRENATAL CARE

The eclamptic patients have been divided into three groups according to the prenatal care which each received. We considered as having had adequate care those patients who registered in the clinic prior to the fifth month and who kept their appointments regularly. The inadequate care group is composed of those who registered late in pregnancy or were irregular in their attendance. By these standards the groups are as follows: adequate care, 40 per cent; inadequate, 37 per cent; and no prenatal care, 23 per cent. In other words, three-fifths of the eclamptic patients had either inadequate or no prenatal care.

TABLE V. INCIDENCE RE PRENATAL CARE

Adequate	40%
Inadequate	37%
None	23%
	} 60%

TREATMENT

The modified Stroganoff or "middle line" plan of treatment has been utilized in this group of patients. We are convinced that early accouchement forc  has no rightful place in the treatment of eclampsia, and on the other hand, we feel that ultraconservative measures should be abandoned if no improvement has followed their use for a period of twenty-four hours.

TABLE VI. ONSET OF LABOR

Spontaneous	62.5%
Medically induced	5.0%
Surgically induced	7.5%
Cesarean section	25.0%
NOTE: 3 patients died undelivered and not in labor	

Sedation has been maintained by the generous use of morphine, fortified by the barbiturates, chloral hydrate, and bromides. Elimination was routinely obtained by gastric lavage followed by magnesium sulphate through the stomach tube, by high colonic irrigations, and intravenous injections of hypertonic glucose solution. Intravenous magnesium sulphate solution (20 c.c. of 10 per cent) was used in approximately half of the group. Hot packs, venesection, and spinal tap were but rarely utilized.

This line of treatment was followed from twelve to twenty-four hours in every case. If the patient improved, expectant therapy was continued. If no improvement was noted, or if the patient grew worse, active means of terminating the pregnancy were undertaken. If the patient was in labor, she was delivered as soon as feasible by forceps or podalic version. If not in labor, the primigravidas were, as a rule, delivered by cesarean section under local anesthesia, and labor was induced either surgically or by rupture of the membranes in the multiparous group.

TABLE VII. METHOD OF DELIVERY

Spontaneous	25.5%
Forceps	40.0%
Version	9.0%
Breech extraction	2.3%
Cesarean section	23.2%
NOTE: Disparity in cesarean section incidence attributable to 3 sets of twins.	

In this series, labor began spontaneously in 62.5 per cent, was medically induced in 5.0 per cent, surgically induced in 7.5 per cent, and cesarean section was performed in 25 per cent. Three patients died undelivered, three, six, and ten hours, respectively, after admission.

MORTALITY

Six of the forty-three eclamptic patients died, giving a mortality rate of 13.9 per cent. This, we feel, compares favorably with the mortality rate of most clinics and is only slightly more than half the generally conceded rate of 25 per cent. Of the six patients who died, three had had no prenatal care and three had had inadequate care.

The deaths from eclampsia comprised 7.5 per cent of the total maternal mortality for the period of this survey.

The uncorrected fetal mortality was 28 per cent.

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DISCUSSION

DR. THADDEUS L. MONTGOMERY.—From June, 1929, to June, 1935, 8,037 patients were delivered under the supervision of the Obstetrical Department of Jefferson Medical College Hospital. The incidence of eclampsia was 1 in 287 cases, 28 patients or 0.34 per cent, a proportion which agrees almost precisely with that stated in the report of the Philadelphia Lying-In Hospital. Of these 28, 12 occurred before labor (43 per cent), 5 during labor (18 per cent), and 11 following delivery (39 per cent). Several of the antepartum cases started in labor a short time after the onset of convulsions and became also intrapartum eclampsias. They have been listed only under the heading "antepartum."

There was little difference in the frequency between white and colored patients, 16 occurring among the former and 12 among the latter. Since the clinical material of the ward service is almost equally divided between white and colored, the difference of number is of no significance. Our statistics confirmed again the point that eclampsia is more common in the primigravid patient than in the multigravid. In our series there were 14 primigravid patients and 14 multigravid patients, while the proportion of registrants in the clinic is 1 to 2½, respectively. It is interesting to note that 4 of the multigravid patients were over thirty-five years of age. Multiple pregnancy occurred in one instance.

Three of the 28 patients were unregistered in the clinic, while 15 were registered, but received inadequate prenatal care through failure to attend regularly the outpatient clinic. Ten received adequate prenatal supervision which should ordinarily prevent the onset of the convulsive phase of toxemia. Therefore, of the 28 patients 64 per cent had inadequate prenatal supervision.

In method of delivery the handling of our eclamptic patient has been somewhat different from that described by the essayist. Seventeen of our patients (60 per cent) delivered spontaneously, 7 (25 per cent) by low forceps, 1 by internal podalic version and extraction, 1 by extraction of the breech, 1 by postmortem cesarean section, 1 by abdominal hysterotomy and sterilization performed at the sixth month and only after the patient had reacted and recovered from the convulsive phase of the toxemia. In 3 patients surgical induction of labor was performed. The latter operation was restricted to preeclampsia which had been under treatment and had temporarily improved, or to eclampsia which had improved after several days of conservative medical treatment.

The duration of labor of these patients was generally quite short. The longest labor recorded was thirty-three hours, in which the ultimate delivery was accomplished by low forceps, both mother and baby surviving.

There were 2 maternal deaths, a mortality rate of 7.1 per cent. The first maternal death was an unregistered patient who was admitted to the ward in a moribund condition, died within a few minutes after admission, and was delivered by a post-mortem cesarean section of a dead fetus. The second patient belonged to the group of inadequate prenatal care, was delivered at home, and died in the hospital of postpartum eclampsia.

The uncorrected fetal death rate was 8 in 28, or 28 per cent. The puerperal temperature morbidity of the mothers was 10 in 28, or 35 per cent, a considerable increase over the general puerperal morbidity of 15 per cent.

Our treatment of eclampsia in its convulsive phase is quite similar to that which has been described. We follow rather closely the methods advocated by Stroganoff, using the morphine and chloral according to the schedule which the latter has suggested. In addition, moderate dehydration is encouraged by the administration of magnesium sulphate by mouth or through the stomach tube, by the institution of a salt-poor diet as soon as the patient is able to take food, by the elimination of intake of fluid to a level below that of the output, by the administration of concentrated solution of glucose, and by the occasional, though infrequent, employment of spinal fluid drainage.

We do not believe that early emptying of the uterus offers any advantage to the patient suffering from eclampsia. We feel that twenty-four hours is too short a time in which to prepare the patient for operative delivery. We feel that it is impossible within this short period to secure sufficient sedation, sufficient unloading of the hydremic nerve and parenchymatous tissue of the individual, and sufficient restoration of the glycogen reserve. We have seen numerous instances in which three, four, and five days have passed before the patient has shown real improvement, and in many of these instances, we have been able to institute induction of labor and subsequent delivery when the convulsive phase has passed. If the emptying of the uterus were of benefit to the eclamptic patient why does such a high percentage of cases occur in the postpartum period, and why is eclampsia as fatal in the postpartum period as it is in the antepartum? While it is true that eclampsia is a metabolic disease attributable to the presence of pregnancy, yet this disease has been accumulating poisons and developing lesions over a considerable period of time, and the emptying of the uterus not only does not immediately relieve them, but in many cases it places a great additional strain upon the overburdened system.

While the results of so small a group of cases as these two offer no dependable basis of comparison, yet the burden of the proof that more radical treatment of eclampsia is preferable falls upon the shoulders of those who advocate it. Either the maternal or the fetal death rate must be decidedly smaller. I had expected, upon review of our statistics, to find that our fetal death rate would be higher, inasmuch as we postpone interference until such can be performed on the less toxic

patient, but on comparison I find our rate of 28 per cent is precisely the same as that reported by the essayists. The maternal death rate in our group of cases, while not, of course, significantly less, is, nevertheless, lower (7.1 per cent).

DR. HENRY LAFFERTY.—We have made a similar study of eclampsia at Hahnemann Medical College Hospital of all cases from 1927 to 1935. During this period there were 11,484 pregnant women admitted to the ward and private services. Forty-two developed eclampsia, an incidence of one in 273 cases. Two-thirds of these cases were in primiparas. Seventeen delivered spontaneously, 22 were delivered operatively, and three died undelivered. There were 4 cesarean sections. The maternal mortality due to eclampsia was 16 per cent; the fetal mortality, 40 per cent. Our therapy in eclampsia is similar to that practiced at the Lying-In and Jefferson Hospitals, a modified Stroganoff.

Peckham in a paper published early in 1935 in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY classified all the cases of eclampsia occurring at Johns Hopkins Hospital into mild and severe, feeling that such a classification was of aid in formulating a prognosis. He gave several criteria indicative of the seriousness of the case, namely, (1) temperature above 103° F., (2) pulse rate above 120, (3) systolic blood pressure above 180 mm., (4) no or very slight edema, (5) deep and persistent coma, (6) 20 or more convulsions. He stated that if two or more of these findings were present, the case was to be regarded as severe or serious. He found no deaths in 102 mild cases, and a maternal mortality of 24 per cent in 103 severe cases. In our series there were 28 mild cases with no deaths due to eclampsia, and 14 severe cases with 7 maternal deaths. The classification of a case of eclampsia into mild or severe is of great aid in prognosis, and the real problem is the treatment of the case classified as severe.

DR. EDWARD SCHUMANN.—I am committed, together with most obstetricians, to the conservative treatment of eclampsia but, occasionally, a case arises in which conservative treatment is followed by a progressive increase in the severity of the disease, and I feel that in some of these patients cesarean section, under local anesthesia, offers the best hope of success. This is particularly true in primiparas, not yet in labor, with undilated and uneffaced cervices and a living and viable child. When such a woman fails to improve after an indeterminate time of conservative treatment, I feel that cesarean section is indicated and should be done.

The published statistics, regarding the very high mortality of section in these cases, are subject to criticism, because in many instances the operation was done in desperation and as a last resort, when the patient was practically moribund. It should be emphasized that I am not an advocate of hysterotomy as treatment for eclampsia, but I feel that one should not be deterred from the employment of this operation when clear indications are present for its use.

DR. JOHN C. HIRST.—May I contribute my summary of statistics on 7,292 consecutive planned pregnancies beyond the twentieth week of gestation. These were collected from the four following sources: (1) the University of Pennsylvania ward, from 1931 to 1934, 3,157 cases with 6 cases of eclampsia and no deaths; (2) the Methodist Hospital ward, 1,070 births with 3 cases of eclampsia and no deaths; (3) the Preston Retreat, from 1931 to 1935, 2,510 births, with 8 cases of eclampsia and no deaths; and (4) personal private cases to date, 1,555 consecutive births, with 3 cases of eclampsia and no deaths. That makes a high incidence in 7,292 planned deliveries with adequate prenatal care, of 1 case in 364 births, but there were no deaths among any of these eclamptic patients.

DR. KIMBROUGH (closing).—I think we have to be on guard against being too confident concerning our statistics when dealing with such small groups of cases.

THE NONPROTEIN, UREA, AND REST NITROGEN OF THE BLOOD DURING NORMAL PREGNANCY AND THE PUERPERIUM

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IT IS generally agreed that normal pregnancy is accompanied by a decrease in blood urea nitrogen. A survey of the literature, however, reveals great disagreement among various investigators as to absolute figures observed during gestation, reported average values ranging from 6.8 to 12.5 mg. per 100 c.c. of blood. As the average urea nitrogen content of the blood in the normal nonpregnant state does not fluctuate between very wide limits, our interest in the reported pregnancy variations at once becomes apparent. Before reliance can be placed on any abnormal findings in the urea nitrogen content of the blood, as has been reported in certain of the toxemias of pregnancy, it becomes essential that the normal pregnancy values be established. Should the wide variations referred to above be corroborated, then too great importance should not be placed upon some of the findings reported in certain of the toxemias. Furthermore, the problem then arises as to the factor or factors involved in bringing about such variations. On the other hand, it is conceivable that differences in method or technique might be accountable for the different values reported. The values referred to have been obtained by the use of different methods, such as that of Folin and Denis, Folin and Wu, Van Slyke and Cullen, or Leiboff and Kahn, or the gasometric urease method of Van Slyke.

For accurate estimation of blood urea nitrogen by any method involving the use of urease it is essential that certain factors, such as the hydrogen ion concentration, the type of buffer used, and the temperature, be carefully regulated. In other words, the determination of urea nitrogen by means of urease is a more tedious procedure than is generally supposed. Considering this point we should like to point out that although practically all of the workers have reported the nonprotein nitrogen to be in the neighborhood of 25 mg. per 100 c.c. of blood, their urea nitrogen values have varied so greatly that we are inclined to believe that some of the discrepancies of the reported urea nitrogen values are due either to difficulties in the analytical technique or to the fact that in some instances the average values for the ten months of pregnancy were based on as few as five cases. Inasmuch as all of the workers, ex-

cepting one who conceded that the procedure he used was inaccurate, have used methods involving urease, we felt that it would be desirable to carry out a series of blood urea nitrogen determinations on normal pregnant women, using a blood filtrate and a method which does not require the use of urease.

METHODS

Filtrates prepared from whole blood by the procedures of Somogyi and Folin-Wu were used for the determination of urea nitrogen and nonprotein nitrogen, respectively. Urea nitrogen was determined by the manometric hypobromite method of Van Slyke and Kugel, and the procedure was frequently checked by analyzing solutions containing known amounts of urea. The method of Folin and Wu was used for nonprotein nitrogen analyses; and the rest nitrogen was calculated as the difference of the two.

By "rest nitrogen" we indicate all the nonprotein nitrogen of the blood excepting the urea nitrogen, in contradistinction to "Undetermined Nitrogen" which not only excludes the urea nitrogen but also the amino acid, uric acid, creatine, and creatinine nitrogen.

In reporting our values we have considered them in respect to the month, as well as the entire duration of pregnancy. The lunar month was calculated from the time of the last menstrual period. In order to have approximately the same number of cases in the various stages of pregnancy, we have considered the second and third, the fourth and fifth, the sixth and seventh, the eighth and ninth months, and the tenth month as individual intervals. Thus, we have 18 cases in the first, 28 in the second, 33 in the third, 28 in the fourth and 25 cases in the fifth group, making a total of 132 cases for the entire duration of pregnancy.

TABLE I. NONPROTEIN NITROGEN

NONPROTEIN NITROGEN MG.	SECOND MONTH	THIRD MONTH	FOURTH MONTH	FIFTH MONTH	SIXTH MONTH	SEVENTH MONTH	EIGHTH MONTH	NINTH MONTH	TENTH MONTH	TOTAL CASES
19-19.9					1					1
20-20.9					1					3
21-21.9				1	2		1			4
22-22.9		1		5	7	3	1		2	19
23-23.9					3	1	3	2	2	11
24-24.9		1		2	2	2	6	1	1	15
25-25.9	1	1	3	3		2	2	5	8	25
26-26.9		3	2	1	6	1	2	1	5	21
27-27.9	3		3	1		1		1	2	11
28-28.9		1		2				1		4
29-29.9	2	1	2	1		1		1	1	9
30-30.9	1	1	1						2	5
31-31.9		1								1
32-32.9										0
33-33.9		1	1						1	3
Total	7	11	12	16	22	11	15	13	25	132
Total	18		28		33		28		25	132
Av. deviation ± Prob. error	28.00 ± 0.39		26.25 ± 0.33		24.04 ± 0.26		24.89 ± 0.22		26.08 ± 0.37	25.62 ± 0.16
Std. deviation ± Prob. error	2.66 ± 0.30		2.65 ± 0.24		2.20 ± 0.18		1.89 ± 0.15		2.74 0.26	2.74 ± 0.11
	First Group		Second Group		Third Group		Fourth Group		Fifth Group	

Table I shows the distribution of the values in regard to the nonprotein nitrogen content of the blood in each month of pregnancy. The total number of cases for the entire duration of pregnancy for each interval of 1 mg. per 100 c.c. of blood is given in the last column of this table.

From an inspection of the frequency table one may conclude that from the second to the sixth month, there is a gradual decrease in the non-protein nitrogen content of the blood and that it then rises during the latter part of pregnancy. A study of the averages confirms this impression. From an average of 28.00 mg. per 100 c.c. of blood in the first group, the nonprotein nitrogen content falls to a value of 24.04 mg. in the third group. From this time it gradually increases and attains an average value of 26.08 mg. in the fifth group. Although this latter value is still somewhat lower than the average for the first group, it is at the same level as that of the second group. Since the range of \pm two sigma (standard deviation) includes 95.4 per cent of the cases we might say that the nonprotein nitrogen range during the period of a normal pregnancy is from 20 to 31 mg. per 100 c.c. blood.

UREA NITROGEN

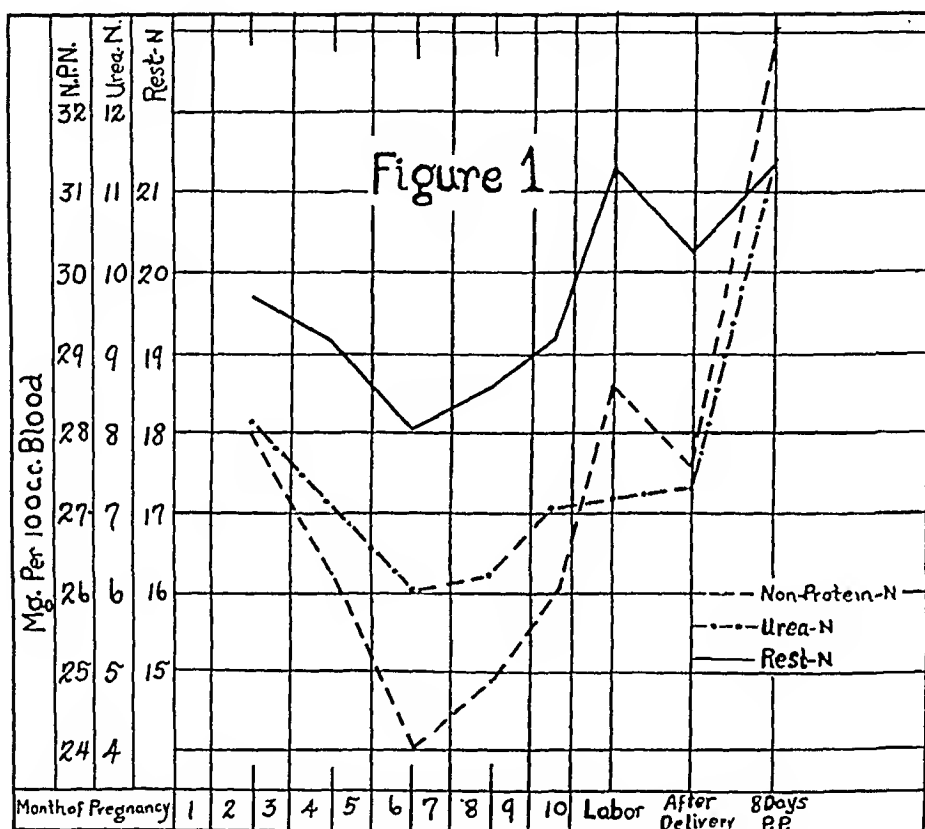
The values for blood urea nitrogen are given in Table II. These, like the non-protein nitrogen values, decrease during the early part of pregnancy reaching the lowest point during the sixth month. However, the blood urea nitrogen does not begin to increase until some time during the eighth or ninth month. By the tenth month it has increased sufficiently to have a value of the same magnitude as the average for the second and third months or the first period. For the entire duration of pregnancy, the average is 6.82 mg. per 100 c.c. of blood with a standard deviation of plus or minus 1.62. Since 94.5 per cent of the values fall within the range of plus or minus twice the standard deviation, we can say that 3.6 to 10 mg. per 100 c.c. of blood is the range for the blood urea nitrogen for the period of normal gestation.

TABLE II. UREA NITROGEN

UREA NITROGEN MG.	SECOND MONTH	THIRD MONTH	FOURTH MONTH	FIFTH MONTH	SIXTH MONTH	SEVENTH MONTH	EIGHTH MONTH	NINTH MONTH	TENTH MONTH	TOTAL CASES
3-3.9						1	1			2
4-4.9				1	2	2	2	3	2	12
5-5.9		1	1	5	10	3	5	3	3	31
6-6.9		4	3	3	7	3	2	1	10	33
7-7.9	2	1	4	2	1	1	4	4	5	24
8-8.9	3	2	1	5	2	1	1	2	2	19
9-9.9	1	1	2						1	5
10-10.9	1	2							1	4
11-11.9			1						1	2
Total	7	11	12	16	22	11	15	13	25	132
Total	18		28		33		28		25	132
Av. deviation \pm Prob. error	8.16 \pm 0.23		7.09 \pm 0.18		6.04 \pm 0.15		6.25 \pm 0.18		7.06 \pm 0.22	6.82 \pm 0.09
Std. deviation \pm Prob. error	1.49 \pm 0.17		1.48 \pm 0.13		1.27 \pm 0.10		1.42 \pm 0.13		1.63 \pm 0.15	1.62 \pm 0.07
	First Group		Second Group		Third Group		Fourth Group		Fifth Group	

REST NITROGEN

When comparing urea nitrogen and nonprotein nitrogen values, we find that they both decrease from the second to the sixth month. The urea nitrogen, however, remains constant until the eighth or ninth month, while the nonprotein nitrogen rises from the sixth month until term. This is clearly shown in Fig. 1. The nonprotein nitrogen falls at a faster rate than the urea nitrogen, resulting in a decrease of 1.64 mg. per cent of rest nitrogen. The rest nitrogen then begins to increase and continues to do so until term, at which time it has reached a value similar to that of the second group.



Studies made by numerous workers on the plasma and serum proteins, the specific gravity, the water content, and the total solids of the blood indicate that there is a dilution of the blood during pregnancy, with the maximum occurring during the sixth or seventh month. In the latter part of pregnancy the water content of the blood decreases as term is approached. From this, we may conclude that the rest nitrogen follows a course approximately parallel to that of plasma volume and that the substance or substances responsible for the changes may be in either plasma or in the cells. In view of the fact that creatine and glutathione are two nitrogenous substances which occur exclusively in the cells, we believe that a study of the concentration of these substances in whole blood in conjunction with the cell volume would be of interest. Work along this line is now being carried out in this laboratory.

THE PUERPERIUM

In Table IV are given the values obtained from the same patients in the last month of pregnancy, during labor, immediately following delivery, and eight days postpartum.

According to the values thus obtained, we find that the nonprotein nitrogen, urea nitrogen, and rest nitrogen, eight days postpartum, are

TABLE III. REST NITROGEN

REST NITROGEN MG.	SECOND MONTH	THIRD MONTH	FOURTH MONTH	FIFTH MONTH	SIXTH MONTH	SEVENTH MONTH	EIGHTH MONTH	NINTH MONTH	TENTH MONTH	TOTAL CASES
13-13.9					1					1
14-14.9				1						1
15-15.9		1			4					6
16-16.9			1	6	3		2	2	2	16
17-17.9	1	3		2	6	2	7	1	3	25
18-18.9	2		3		4	2	2	3	8	24
19-19.9	2	2	1	1	2	6	2	4	3	23
20-20.9		1	4	4	1	1	1	1	4	17
21-21.9	2	2	1	1	1			2	2	12
22-22.9		1	1	1			1			3
23-23.9			1						2	3
24-24.9		1								1
Total	7	11	12	16	22	11	15	13	25	132
Total	18		28		33		28		25	132
Av. deviation ± Prob. error	19.67 ± 0.37		19.16 ± 0.31		18.03 ± 0.20		18.60 ± 0.19		19.18 ±0.28	18.81 ±0.12
Std. deviation ± Prob. error	2.17 ± 0.24		2.44 ± 0.22		1.72 ± 0.14		1.52 ± 0.14		2.06 ±0.19	2.00 ±0.08
	First Group		Second Group		Third Group		Fourth Group		Fifth Group	

markedly increased over the corresponding values for the tenth month. We do not wish to stress our findings at parturition, inasmuch as we have only a few cases. However, from the averages we may tentatively say that the nonprotein nitrogen decreases during parturition with a corresponding lowering of the rest nitrogen. The urea nitrogen is apparently unaltered. Further study of this point is necessary before we could draw definite conclusion. In connection with this point it would be very interesting also to follow any changes that might occur in cell volume and glutathione.

DISCUSSION

Earlier in this presentation we have pointed out that values averaging from 6.8 to 12.5 mg. of urea nitrogen per 100 c.c. of blood have been reported as the average for the ten months of pregnancy. In Table V are given the findings of various authors. From this table one may readily see that only 3 of those listed had 50 or more analytical figures on which to base their conclusions. We shall therefore compare our results with these three only.

TABLE IV

CASES	TENTH MONTH			DURING FIRST STAGE			AFTER THIRD STAGE			EIGHTH DAY POSTPARTUM		
	N.P.N.	UREA N.	REST N.	N.P.N.	UREA N.	REST N.	N.P.N.	UREA N.	REST N.	N.P.N.	UREA N.	REST N.
Case 1 T. S.	21.40	4.70	16.70	29.10	6.10	23.00	26.60	6.20	20.40	36.00	10.10	25.90
Case 2 V. M.	26.4	10.1	16.3	31.2	8.8	22.4						
Case 3 C. D.	25.0	6.8	18.2	34.9	9.5	25.4	36.4	11.1	25.3	44.5	21.2	23.3
Case 4 M. H.	30.0	7.1	23.0	31.4	7.2	24.2	27.2	7.4	19.8		7.2	
Case 5 E. T.	23.3	6.4	16.9	29.6	8.3	21.3				30.3	9.3	21.0
Case 6 M. D.	25.1	6.7	18.4	24.0	6.4	17.6	26.0	7.5	18.5	32.1	11.1	21.0
Case 7 R. K.	25.5	6.7	18.8	31.1	6.8	24.3	30.0	7.0	23.0			
Case 8 G. C.				22.2	5.1	17.1	24.7	5.9	18.8	39.7	13.0	26.7
Case 9 E. P.				24.0	6.9	17.1	22.5	6.5	16.0	32.2	11.1	21.1
Case 10 E. C.	27.1	7.7	19.4							30.8	10.7	20.1
Case 11 P. W.	33.3	9.6	23.7							29.1	9.4	19.7
Case 12 B. A.	26.9	5.7	21.2							30.6	8.9	21.7
Case 13 A. M.	25.0	6.5	18.5							33.3	13.2	20.1
Case 14 C. P.	30.8	11.1	19.7							32.1	13.3	18.8
Case 15 M. A.	22.3	4.6	17.7							29.0	8.8	20.2
Case 16 F. A.	25.8	6.4	19.4							30.9	11.2	19.7
Case 17 J. B.	25.4	7.1	18.3							33.1	13.2	19.9
Case 18 E. P.	23.5	6.7	18.8							32.4	10.7	21.7
Average	26.04	7.12	19.02	28.61	7.27	21.38	27.63	7.37	20.26	33.14	11.40	21.39
Std. dev.	2.96	1.44	2.05							2.92	1.57	2.56

Our findings are in complete agreement with those of Folin. The non-protein and urea nitrogen curves follow rather closely those of Bunker and Mundell, excepting that our urea nitrogen values are considerably lower. We concur in the conclusion of Caldwell and Lyle

TABLE V

AUTHOR	YEAR	NO. CASES	N.P.N.	UREA N.	REST N.	UREA N.
						N.P.N.
Farr, Williams	1914	10	25.6	10.0	15.6	0.41
Slemons and Morris	1916	35	25.2	10.4	14.8	0.44
Folin	1917	100	less than 30	4 to 9		0.20 to 0.35
Killian and Sherwin	1921	5	23.0	10.4	12.6	0.45
Caldwell and Lyle	1921	150	29.7	11.5	18.5	0.39
Hellmuth	1923	8	24.0	7.7	16.3	0.32
Bunker and Mundell	1924	52	25.0	12.5	12.5	0.50
Hurwitz and Ohler	1932	4	30.0	6.8	23.2	0.23
Dieckmann	1935	23	23.8	12.2	11.6	0.51

in that, "In normal pregnancy, as compared with the nonpregnant state, we find a low total nonprotein nitrogen, low urea nitrogen and a very low ratio of urea nitrogen to the total nonprotein nitrogen."

SUMMARY

The nonprotein, urea, and rest nitrogen were determined in 163 blood specimens, obtained from normal pregnant women at different periods of gestation, during labor, and on the eighth day postpartum. Although nitrogen determinations were not performed on any one patient throughout the course of her pregnancy, we believe that the data we have obtained warrant the following conclusions regarding normal gravidity, especially as we have given due attention to the statistical distribution of our figures.

CONCLUSIONS

1. The nonprotein nitrogen of the blood decreases during the first six months of pregnancy from the average nonpregnant values of approximately 30, to 24 mg. per 100 c.c. of blood.
2. During the last four months of pregnancy the nonprotein nitrogen increases steadily until one week postpartum when it averages 33 mg. per 100 c.c. of blood, being about 26 mg. at term.
3. The urea nitrogen concentration diminishes during the first six months from the usual nonpregnant value of about 14 mg. to a value of 6 mg. per 100 c.c. of blood; and then maintains a constant level until the eighth or ninth month, when it begins to rise, having an average value of 7.12 mg. at term and 11 mg. per 100 c.c. blood on the eighth day postpartum.
4. Due to the fact that the nonprotein nitrogen falls and rises more rapidly than the urea nitrogen, the rest nitrogen falls during the first

six months of pregnancy to a value of 18.02 mg. per 100 c.c. of blood and then increases during the latter part of pregnancy, being 19.18 mg. at term. It is further increased during the first week postpartum, reaching a value of 21.39 mg. on the eighth day of the puerperium.

5. Although it is quite evident that a change in the rest nitrogen is not necessarily accompanied by a change in the $\frac{U.N.}{N.P.N.}$ ratio, our figures show that the urea nitrogen to nonprotein nitrogen ratio is decreased during pregnancy, being 0.25 during the sixth or seventh month and 0.27 at term. The normal nonpregnant value for this ratio is approximately 0.50.

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Patoir, André, and Patoir: Poisoning With Apiol, Paris méd. 25: 397, 1935.

Apiol is widely advertised as a so-called emmenagogue and extensively used as an abortifacient. It is supposed to be nontoxic though occasionally cases have been reported where mild poisoning had followed the use of this preparation either in large doses or for a long time. More recently new attention has been directed toward this drug by the reports of instances of polyneuritis and nephritis. A polyneuritis epidemic in the U. S. a few years ago following the use of Jamaica rum had been definitely traced to its contents of triorthocresyl phosphorous ester. A similar sudden accumulation of cases of polyneuritis in Germany has been found to be due to extensive use of creosote phosphate in pulmonary affections. The apiol polyneuritides observed in France (also in U. S.) revealed in their symptomatology and course a striking similarity to those previously mentioned. This is probably satisfactorily explained by the fact that in various apiol preparations on the market triorthocresyl phosphorus has been discovered.

After a variable delay the first symptoms of intoxication appear in the legs, especially toes, gradually proceeding to paralysis. About a week later the hands become involved. If medication is not stopped, serious and even fatal hepatonephritis will develop. Abortion actually results not as a direct result of the apiol but as part of the general impairment of the patient through renal breakdown, emaciation, often fever.

For obvious reasons only a few even of the serious cases are reported. The free sale of apiol should be prohibited.

HUGO EHRENFEST.

THE SIGNIFICANCE OF FETAL HEART TONES IN ABLATIO PLACENTAE*

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THE individual life span is all too short for anyone to experience, in practice, all obstetric possibilities. Nor is it within the bounds of a single obstetric text, or system of obstetrics, to describe, to prognosticate, and to treat all obstetric conditions with their numerous variations.

A text, therefore, must represent the experiences of the author, or editor, together with such facts and figures as are gleaned from preceding literature and other sources of information. Too often, however, a statement is handed down from one writer to another to be accepted, and passed on, as fact, without challenge or compromise.

It is by way of friendly challenge that this subject, "The Significance of Fetal Heart Tones in Ablatio Placentae," is presented for the first time, and only after a careful search of the literature had revealed that an evaluation of the fetal heart tones in ablatio had never, apparently, been published.

On Sept. 20, 1901, Holmes¹ presented before this society his Inaugural Thesis, "Ablatio Placentae," based on the study and analysis of 200 cases. In this thesis, which today, thirty-four years later, still retains its position as the classic on ablatio placentae, Holmes warned that "The condition of premature detachment of the normally situated placenta is one which has been given insufficient attention by obstetricians; that its frequency has been greatly underestimated; its mortality judged too high, and that its treatment is still a moot question."

In concurring with Holmes, with some degree of modification and reservation, attention might well be directed to the literature dealing with ablatio placentae, from which it is evident that too trivial consideration is accorded to the fetal heart tones, although these have a definite importance in this complication.

We are only too familiar with the almost universal expressions of authors, who dismiss the fetal heart tones in placental separation with such statements as "The fetal heart tones disappear," "after a period of unusual fetal activity the heart tones cease," or in extremes, "the heart sounds are not heard," or "are absent."

*Read at a meeting of the Chicago Gynecological Society, February 21, 1936.

Williams² (*Obstetrics*) states, "In concealed hemorrhage . . . as the child is dead, auscultation gives negative results. . . . When the premature separation of the placenta occurs at the time of labor . . . the hemorrhage is usually external and the fetal heart sounds suddenly become imperceptible." He makes no other reference to fetal heart tones.

DeLee,³ discussing symptoms, diagnosis, and treatment, refers to fetal activity and fetal heart tones as follows: "During pregnancy . . . the woman says that the child is not felt, but that it was subject to violent movements at the onset of the accident. Very seldom can the fetal heart be heard, and under such conditions a partial separation of the placenta must be assumed. . . . During labor . . . the accoucher, attentively observing the fetal heart tones, discovers the agitation of the child." In diagnosis and differential diagnosis he refers only to "absence of fetal heart tones" and "cessation of fetal movements." Under treatment he states, "If the hemorrhage continues, and especially if the fetal heart tones become irregular or slow, a diagnosis of abruption is now made, and the child should be delivered without delay. The accoucher must sit by his patient watching every change in her condition closely. . . ."

Hirst⁴ makes no mention of fetal heart sounds, except to say, in his differential table, that they usually disappear. Vaux⁵ makes no mention of fetal heart sounds. Cooke,⁶ writing the section on "Premature Separation of the Placenta" in Curtis' *System of Obstetrics and Gynecology* says: "The absence of fetal heart sounds may or may not be of significance. . . . A marked and progressive increase or decrease in the fetal heart rate followed by cessation of the sounds, is seriously suggestive of fetal death. . . ." Holmes,⁷ in the chapter on *Ablatio Placentae* in Davis' *Gynecology and Obstetrics*, writes: "If the fetal circulation is cut off suddenly by a widespread placental separation, the sudden asphyxia will cause violent fetal movements, then the quiet of death will supervene. If the arrest of circulation is slow, the marked activity of the fetus will be absent, and the child gently passes into death."

Treatises on premature separation of the normally implanted placenta, reviewed in the literature, present about the same brief summation regarding fetal heart tones as these citations from a representative group of obstetric works. Davis and McGee's⁸ statements relative to the fetal heart contain probably the greatest significance of any found in the literature. They say that "On auscultation of the fetal heart one finds evidences of fetal asphyxia demonstrated by an irregularity in rhythm or a decrease in rate," and under diagnosis, "The diagnosis of partial abruptio placentae can be made by the sudden change in the character of the labor, the external hemorrhage, and the signs of fetal asphyxia as indicated by the slowing of the fetal heart rate." Discussing treatment these writers report cases of sudden change in character of labor, external hemorrhage, tenderness, early uteroplacental apoplexy, and decreased fetal heart rate, adding "this is the only case of this kind in which we were able to deliver a live baby."

That last statement strikes at the keynote of this paper. It strikes at the veritable cause of the high mortality rate of mother and fetus. It was almost too late. How many times are we almost, if not actually, too late to save the mother only, when by earlier recognition both might have been living!

The literature teems with discussions and reports of cases where one of three conditions prevailed: first, the patient came under observation too late; the sequence of events was too fulminating; or, our diagnosis was either too slow or treatment was deferred through too much "watchful expectancy" in which the attention was directed toward the rapidly failing condition of the mother, and with little or no regard for the fetal heart tones which present one of the earliest and most significant signs.

Not only do the fetal heart tones present the *earliest* indication in premature separation of the placenta, but they are always altered in so definite a manner as to direct our suspicion positively toward a placental detachment. I desire at this time to present an adequate evaluation of the significance of the heart tones in this condition as to attract more careful and deeper study in this most serious obstetric condition.

Besides the lack of a proper evaluation of the fetal heart sounds, the term "abruptio placentae" used by some authors and writers, is without a doubt directly conducive to a deferred diagnosis and resultant delay in treatment with a consequent higher mortality of mother and fetus. The word abruptio in its literal sense conveys the idea of suddenness, haste, and a forcible breaking off. Abruptio may be defined as a sudden breaking off, a violent separation of bodies and as unceremonious. Therefore, abruptio placentae defines etiologically only one, and the smallest, group of premature placental separations, namely those which occur suddenly and completely in some instances, but even in these the process is not a sudden breaking off, but rather an orderly process of cleavage by hemorrhage between placenta and uterus. Nor is it unceremonious. Previa, too, when bleeding, is a process of separation.

Stormy as it may be, there is probably no condition in obstetrics which is so ceremonious in its course as ablatio placentae. The event pursues a definite and methodical progression of incidents, which occur in an identical sequence without regard to the time factor involved, whether it be five minutes or five hours.

This sequence may be indicated as,

1. Hemorrhage (or separation).
2. Placental separation with increasing hemorrhage (both progressive).
3. Decreased oxygenation and increased fetal carbon dioxide retention.
4. Fetal embarrassment with compensatory acceleration of fetal heart rate.
5. Fetal heart compensation to maximum tolerance.
6. Asphyxia with decreasing fetal heart rate.
7. Placental separation complete either before, or after.
8. Fetal death, quiet or violent.

In considering singly this orderly and significant program in such a catastrophe it matters little which precedes, the hemorrhage or the separation. Either could produce the other; also, either could result from the other. Both are progressive, and as the all-important time factor

advances, the fetus responds with an acceleration of the heart rate. This occurs at a point somewhere between zero and a separation of about one-fourth of the placental area and agrees in proportion to the amount of separation and the temporal factor which may be referred to as time.

The acceleration of the heart rate is a regular physiologic process which can be expressed in figures which correspond to the degree of separation and time, and will be so expressed hereafter. Any separation of placenta, however slight, obviously alters the oxygen and carbon dioxide exchange between placenta and placental site, or between fetal and maternal organisms. The slight crescentic separations so familiar at the margin of placentas do not sufficiently alter the $O_2 - CO_2$ exchange as to affect the fetal heart rate. This group should be considered as comprising those of lesser clinical importance which Holmes⁹ refers to as occurring once in 200 cases. They deliver spontaneously and without evidence of previous separation until the placenta is inspected after the third stage of labor and the crescentic area of the marginal clot is discovered.

As placental detachment increases, the oxygen-carbon dioxide exchange is so altered as to produce fetal heart embarrassment, to which the fetus responds with a compensatory acceleration in the heart rate. Since the oxygen-carbon dioxide balance is directly dependent upon the area of placenta and placental site, that balance will be impaired in direct proportion to the amount of placenta detached. The fetal requirements for oxygen and its necessity of carbon dioxide elimination remain rather constant for a given period. Since the fetal circulation is the sole agent for oxygen delivery and carbon dioxide dissemination, that circulation should and does speed up in a direct relation to the ever diminishing available area of placental attachment. This constitutes a compensatory phase in which the fetal heart becomes continuously more rapid until the functioning placental area becomes so small that it no longer suffices to maintain an oxygen-carbon dioxide balance. Oxygen is deficient, CO_2 overwhelming, asphyxia ensues, and the fetal heart rate slows down with advancing detachment until ablation nears or reaches completion. In this phase of asphyxia, characterized by a failing heart muscle, and an ever slowing fetal heart rate, fetal death occurs quietly in prolonged cases, and with violent fetal activity where ablation is rapid.

There are two exceptions, and probably only two, to this uniform scheme in ablation. The first is that group of cases in which the time element is too great in any one phase for the fetal heart muscle to withstand the exhausting rapidity of its effort to exchange oxygen and carbon dioxide. The second comprises a small number of cases in which the hemorrhage is external quite early and the egress of blood so rapid that the placental site is drained too swiftly for the fetus to acquire oxygen in spite of its circulatory activity.

The physiologic response of the fetus to ablatio is uniform and uninterrupted from beginning to end. The case reports will place a numerical value upon these physiologic responses, which evaluation, it is hoped, will inspire more scientific attention than mere watchful expectancy, and will demand earlier diagnosis and more prompt interference.

On Nov. 7, 1932, Dr. J. K. McQuarrie referred the case which prompted a study of fetal heart tones in ablatio placentae. This case was such as to make it immediately obvious that the heart tones could and should be used to great advantage as a diagnostic and prognostic aid. Then it happened that in the following three years eight more such cases, all of the grave type, came to observation, and these, with the first one mentioned, have made the completion of findings possible in all stages of placental separation.

CASE REPORTS

CASE 1.—Mrs. K., white, para i, aged twenty-five. Pregnancy normal, highest blood pressure 116/70. Urinalysis negative throughout. No bleeding or toxic symptoms during pregnancy. Entered hospital at 8 A.M. Dec. 7, 1932, in labor at term, with history of membranes having ruptured at 6 o'clock. After rectal examination which revealed no dilatation and head high, the patient was prepared for delivery. The maternal pulse was 76, fetal 140. At 9 A.M. a visible, external hemorrhage occurred and the amount was estimated at 50 c.c. There was no pain. The mother's pulse was 88, fetal 140. At 9:40 A.M. the dilatation was 1 cm. At 10:40 the fetal heart tones were 140. Rectal examination revealed dilatation still 1 cm. No boggy mass, no placental pulsation, and no undue thickness of tissue could be palpated between the rectal finger and the presenting head. No bleeding followed the rectal examination. Ablatio placentae was diagnosed.

At 11:20 A.M. a second hemorrhage occurred, this time between 50 and 100 c.c. and again without pain, other than the labor pains which were weak, irregular, and unproductive. Dilatation was still only 1 cm. at 11:30 A.M., but the fetal heart tones had increased in rate to 160. They were strong, full, and rapid. The mother's pulse was now 92, and it was observed that while the uterus was not painful, it was tender, and now failed to relax as completely as formerly, though not of ligneous hardness.

The patient and husband were told that while the baby was markedly embarrassed, it was in good condition (barring ateleetasis) but that without interference, and with a failure of progress, that the baby would succumb to the placental separation, which might later require cesarean section for a dead baby in order that hemorrhage might be checked in behalf of the mother.

Low cervical cesarean operation was performed and a live infant delivered. It cried immediately, as it was overloaded with CO₂ but delivered still in the stage of compensation.

Lest bleeding and the first uterine contraction should produce further placental separation the infant was immediately intrusted to an associate, and the uterus was invaded to determine the degree of placental separation that had caused the fetal heart to increase from 140 to 160. The placenta was found high on the posterior wall of the uterus, with one-fourth to one-third of its lower portion separated. There were some recent clots and about 350 to 400 c.c. of fluid blood between the uterine wall and the placenta and membrane.

There had been no injury, yet a painless hemorrhage had taken place, one just as causeless, if such can be said, as in placenta previa, yet not a placenta previa. Known duration of separation was three hours fifty-eight minutes.

Recovery was uncomplicated. Mrs. K. has had one normal delivery since, and one precipitate in an ambulance en route to the hospital.

CASE 2.—Mrs. S., white, para ii, aged twenty-five years. Prenatal care uneventful. Term date estimated at March 8, 1933. Highest blood pressure 120/70. Urinalysis normal. No toxemia. Fetal heart tones last prenatal visit 136, March 3, 1933.

The next day, March 4, 1933, labor began at 6 P.M. Patient entered hospital at 7 P.M. She had about 100 c.c. of external bleeding. Placenta previa was diagnosed by the interne. This was corrected by myself, and diagnosis, rectally and by history, of ablatio placentae was made.

Fetal heart tones on admission were 132, at 9 P.M. they were 150 and dilatation was complete. There was no pain except from the contractions but the uterus was tender. Delivery was spontaneous at 9:35 P.M. The placenta was expelled at 9:40 P.M. with a blood loss of 300 c.c. One-fourth of the placental surface was covered with clot in evidence of the area detached.

The known duration of the separation was two hours and thirty-five minutes. The uterus, while it failed to relax completely between pains, never even approached the so-called ligneous hardness.

The newborn respirations were spontaneous and prompt.

CASE 3.—Mrs. B., white, para ii, aged thirty-three years. This patient was seen seven times prenatally. Urinalysis was normal. The highest blood pressure was 118/70. The fetal heart tones during pregnancy were 136.

On Nov. 8, 1933, at 2 A.M. she called the doctor to say she had been awakened by a severe hemorrhage. She was not in labor, had no pains, and was three or four weeks from term.

Mrs. B. entered the hospital an hour later, though not in labor nor in pain, but with what the nurses described as a large amount of bleeding. Examination at 3:10 A.M. revealed no dilatation, head floating, O.L.A., fetal heart tones 162. The interne made a diagnosis of placenta previa.

Examination revealed fetal heart 170 and maternal pulse 148, respiration 24, a uterus tender but not painful, not fully relaxing between pains, but not ligneous by any means.

Low cesarean operation was performed at 5 A.M. and a live viable baby was delivered. The placenta was high on the posterior wall of the uterus, with one-half its area separated.

The known duration of ablatio here was three hours.

CASE 4.—Mrs. D., white, para ii, aged thirty. Seen seven times prenatally. Urinalysis normal. Last prenatal visit fetal heart tones were 136, blood pressure 98/54, April 2, 1934.

On April 6, 1934, patient phoned at 6:30 A.M. that she had had some bleeding since 6 A.M., but no pain. She was then beginning the seventh month of gestation.

She was admitted to the hospital two hours later though not in labor and still bleeding without any pain.

At 8:05 A.M. the head was floating, the os was undilated, and the uterus was tender, somewhat firm and not hard. Fetal heart tones were 170 to 180, bag of waters intact, maternal pulse 94, and respiration 18. Fetal heart tones began to decrease and by the time of the operation had slowed to 120. The phase of asphyxia was in progress. The mother's condition was good but while fetus was premature, labor did not begin and severity of signs and symptoms made it apparent that section might be necessary, in absence of labor, to control blood loss of mother.

Section was done at 9:30 A.M. and a small premature, moderately asphyxiated infant of three and three-fourths pounds was delivered. The placenta was high on posterior wall of the fundus and separated in its lower one-half.

The known duration of the ablatio was three hours and thirty minutes.

The baby respired but succumbed to prematurity eight hours after delivery.

CASE 5.—Mrs. S., white, para i, aged thirty-six, was a known diabetic for eight years. She had had two amputations of right leg, and was taking maintenance doses of U 10 insulin morning and evening. She was advised against childbearing but was determined to become a mother. The last menstruation began Feb. 1, 1933, which would bring her to term about Nov. 8, 1933.

She had slight bleeding Sept. 17, 1933, at about 6 P.M. (fluid blood, not a bloody mucus). She was in labor and the fetal heart tones were 160 and good quality. Immediate hospitalization was advised.

She entered the hospital Sept. 17, 1933, at 8:25 P.M. with profuse bleeding and a blood pressure of 180/105. Abdomen was tense. The fetal heart tones were reported by the interne as 140 and were never heard again. This decrease in rate over that of two hours previous was evidently due to the asphyxia phase of placental separation. The first stage was five hours eleven minutes, second stage forty-five minutes. The placenta was expelled with the baby; separation had been complete. The patient, mentally uncertain on admission, was semicomatose at delivery but recovered.

Known duration of separation was six hours sixteen minutes.

CASE 6.—Mrs. A., white, para i, aged twenty-five. Last menstruation June 1 (?), 1934, term March 10 to 15, 1935. Fell on stairs Feb. 27, 1935. Fetal heart tones during pregnancy 144.

March 4, 1935, she had a severe headache at 8 A.M., and at noon a hemorrhage occurred and was estimated by patient to be easily one-half teacup in amount. Headache ceased immediately after onset of bleeding. Hemorrhage was painless and followed in ten minutes by a second painless and so-called causeless hemorrhage, which did not cease entirely until delivered. There was no pain until after arrival at the hospital at 3:15 P.M. on March 4.

Bright red blood appeared externally. Fetal heart tones were absent. Maternal pulse was 100. The first examination of patient was at 5:30 P.M. when bleeding was moderate, uterus larger than normal, tender and of ligneous hardness. Diagnosis of ablatio placentae was made and cesarean section advised, in spite of dead fetus, to control bleeding since the irregular labor had effected no progress. Couvelaire uterus was also given serious thought. Uterine pain began three and one-half hours after first hemorrhage. Labor pains began three and one-fourth hours after first hemorrhage.

Section was done and the fetus was found to be dead, placenta completely separated, and small subserous hemorrhagic areas were found over placental site on anterior wall of uterus. The uterus was not removed.

CASE 7.—Mrs. O., white, para ii, aged thirty-six years, was toxic in first and present pregnancy. Albuminuria varied from slight to moderate with some casts. Toxemia was on renal basis. Blood pressure increased from 110/70 to 160/80. Fetal heart tones last prenatal recording were 144. She entered hospital at 2:15 P.M. April 8, 1936, and was examined at 2:30. There were no fetal heart tones. Cervical dilatation was 7 cm., and patient was sent to the delivery room. Membranes ruptured at 3:25. Delivery occurred at 3:32 P.M. Placenta was retained by a contraction ring and had to be removed. It showed evidence of old separation over three-fourths of its area, but without bleeding. There was no history of bleeding, no bleeding in labor, and no hemorrhage with the delivery. Fetal death evidently

was the primary event, followed by thrombosis or agglutination of the vessels and placental separation without hemorrhage.

Duration of separation could not be known but life was not demonstrable two days before delivery.

CASE 8.—Mrs. M., white, aged thirty-eight years, para iii. Last menstruation was Nov. 14, 1934, quickening April 4, 1935, term date Aug. 21, 1935. Prenatal care was without incident, the urinalyses and blood pressure were normal, the last being 122/68. Fetal heart tones at the last visit were 136, and in R.L.Q.

Mrs. M. was admitted to the hospital at 3:30 A.M. July 9, 1935, in labor, having pains every three to five minutes, which lasted forty to fifty seconds. The interne on duty made his examination at 3:45 A.M. and reported the position obscured by a moderate polyhydramnios. Fetal heart tones were reported not heard. The patient was examined more carefully at 4:10 A.M. when the dilatation was between 7 and 8 cm. At this time a heart rate of 74 was observed and was assumed to be the mother's. Subsequent delivery of the baby proved, however, that this was the fetal heart tones, as the pulsation of the cord at delivery was at rate of 74, and auscultation over baby's precordium revealed a rate of 74. Reference then to the nurse's record showed mother's pulse on admission to have been 90, with other recorded rates of 92 and 84. At no time was the mother's pulse recorded as low as 74, until twenty-four hours after delivery. Palpation of the mother's pulse at time of listening for fetal heart tones would have eliminated this error of reporting them as absent.

Breech extraction was at 6:42 A.M. The baby was five to six weeks premature and weighed 5 pounds 3 ounces. It was partially asphyxiated, had a very extensive spina bifida, open beyond repair, and succumbed to its prematurity, asphyxia, and malformation within an hour after delivery. Autopsy showed numerous other anomalies.

The placenta, delivered immediately after the baby, showed the opening in the membranes sufficiently far from the placenta to rule out marginal, or low implantation. Old clots and discoloration of the maternal surface of the placenta indicated that this organ had been detached over three-fourths of its area for a considerable time previous to delivery. The uterus was never of ligneous hardness but did not completely relax between pains.

Known duration of ablatio was three hours forty-two minutes.

This series of cases gives me positive evidence of the value of the fetal heart tones in ablatio placentae from the standpoint of diagnosis, prognosis, and guidance in treatment. Often cases have a negative value, as well as positive. In this category it is well to cite two cases in which the constancy of the fetal heart rate proved the deciding factor in ruling out placental separation.

CASE 9.—Mrs. D., white, para ii, aged twenty-eight years, has a single prenatal record extending over a period of twelve months and eight days. The early part of this record discloses a history varying from spotty to free bleeding at frequent intervals. Subsequent history and examination led to the conclusion that spontaneous abortion occurred at about two to two and one-half months. Events that followed proved this patient to have become pregnant immediately after aborting. The first six months of this second pregnancy (her third) was rather free of any bleeding. The last trimester was productive of two hemorrhages varying from reported one-fourth to one-half cup volume. The fetal heart tones were taken at home and on subsequent frequent office visits in both instances of hemorrhage. They were found to be entirely uninfluenced in their rate by either hemorrhage, showing no interference, therefore, in the oxygen-carbon dioxide exchange between fetus and

mother. This ruled out placental separation and rectal examination failed to reveal a placental mass in the pelvis, which ruled out placenta previa. There was no cervical polyp or varix. The placenta, delivered at term June 9, 1935, showed no signs of even slight separation and no evidence of injury or accident to the marginal vein. The origin of hemorrhage, in this case, was undetermined.

CASE 10.—Mrs. W., white, aged thirty-three, para ii, gave a history of rather severe hemorrhage while walking about her home, a little before the seventh month. At this time her attending physician made a tentative diagnosis of placenta previa or possible ablatio placentae. The bleeding ceased in compliance with his order of complete rest in bed. There was no recurrence of bleeding. After freedom of hemorrhage for approximately three weeks, internal examination revealed the absence of any placental mass within reach of the examining fingers. The fetal heart tones at the time of hemorrhage and throughout subsequent prenatal visits were within the range of 136 to 140, this difference being only an amount that could be accounted for by variation in the count of one beat per fifteen seconds. The fetal heart tones and internal examination seemed, in this instance, to rule out both placental detachment and placenta previa.

Mrs. W. entered the hospital at 10:45 P.M. May 26, 1935, in labor without bleeding, blood pressure 110/88. The fetal heart tones were 136, position L.O.A., dilatation 1 to 2 cm., pains slight and at five- to ten-minute intervals. Labor progressed normally, dilatation being complete at 10:45 A.M., delivery at 11:44 A.M. The placenta was expelled at 11:49 A.M. There was no unusual bleeding in labor; the heart tones remained normal. The site of rupture of the membranes indicated that the placenta had been situated high in the uterus and gave no evidence of any separation. The perineum and vaginal mucosa were markedly varicose. This condition, no doubt, was the source of the hemorrhage at seven months, at which time observation of the fetal heart tones relieved a tense situation.

In reviewing these cases it would seem that the greatest practical value in studying the significance of fetal heart tones would be derived by classifying them in accordance with their degree of separation. This classification must, of course, at first be arbitrary, but it would seem that there could hardly be a simpler scheme than that of using the fractional area basis of detachment as expressed in these case reports, to compare with the heart rate acceleration. Since both extreme and intermediate variables of rate and area separation are represented in these cases, they might be accepted as a standard of future investigation. These values were determined by steadfast watching of every phase of each individual case, together with positive determination of the degree of placental separation at delivery.

In this way it can be shown that a definite degree of placental separation is associated with a rather definite acceleration in the fetal heart rate and the following values obtained. Taking as a basis a normal case with average fetal heart tones of 136 to 140 and the placenta completely attached, the separating of one-fourth to one-third of the area would lead one to expect the fetal heart tones to be 160 to 170; while with one-half separation and fetal heart tones of 180 to 190, at which point, the time factor considered, the fetus passes from a compensation phase into a phase of asphyxia. When the fetal heart tones decrease with three-fourths separation of placenta from 90 to 70 fetal death will occur before, at, or immediately after complete detachment. This process may

TABLE I. TABULATION OF CASE REPORTS

CASE	AGE	PARA	HEM.	PAIN	TENDER- NESS	UTERINE FIRMNESS	F. H. T.		B. P.	PLAC. SEP.	DURATION OF PLAC. SEP.	BABY	
							PREG.	HOSP.				BORN	L--LIVED D--DIED
1-K	25	i	V.E.	0	+	Sl.	140	160	116/70	$\frac{1}{2}$ - $\frac{3}{4}$	3 hr. 58 min.	A	L
2-S	25	ii	V.E.	0	+	0	136	150	120/70	$\frac{1}{2}$	2 hr. 35 min.	A	L
3-B	33	ii	V.E.	0	+	Sl.	136	162	118/70	$\frac{1}{2}$	3 hr.	A	L
4-D	30	ii	V.E.	0	+	Sl.	136	170	98/54	$\frac{1}{2}$	3 hr. 30 min.	A	Premature
5-S	36	i	V.E.	+	+	0	?	160 → 140	180/105	C	6 hr. 16 min.	S	D —
6-A	25	i	V.E.	+	+	Lig.	?	0	?	C	3½ hr.	S	—
7-O	36	ii	V.E. O.	0	0	0	144	0	110/70 to	C	3½ hr. ?	S	—
8-M	38	iii	V.E.	0	+ sl.	Sl.	136	74	160/80 122/68	$\frac{3}{4}$	3 hr. 42 min.	A	Asphyxia D
9	?	M	V.E.	0	+	Sl.	?	160	?	?	?	A	Deformity L
10	?	M	V.E.	0	+	Sl.	?	150	?	?	?	A	L
												70% A 30% S	50%

70% M 90%
30% Pr.

involve five minutes or five hours and will obviously present some variations, depending upon the elapsed time occupied by any phase along this uniform line of events.

For instance, one case had fetal heart rate of 70 with three-fourths of the placenta separated, while in another the heart tones were absent with the same degree of detachment, showing that, after all, there is a limit beyond which the fetal organism can no longer compensate for a given degree of placental detachment.

In this study we have watched the heart accelerate, and at delivery determined the area of placental detachment in order to form a logical association of these two phenomena. The practical application now fol-

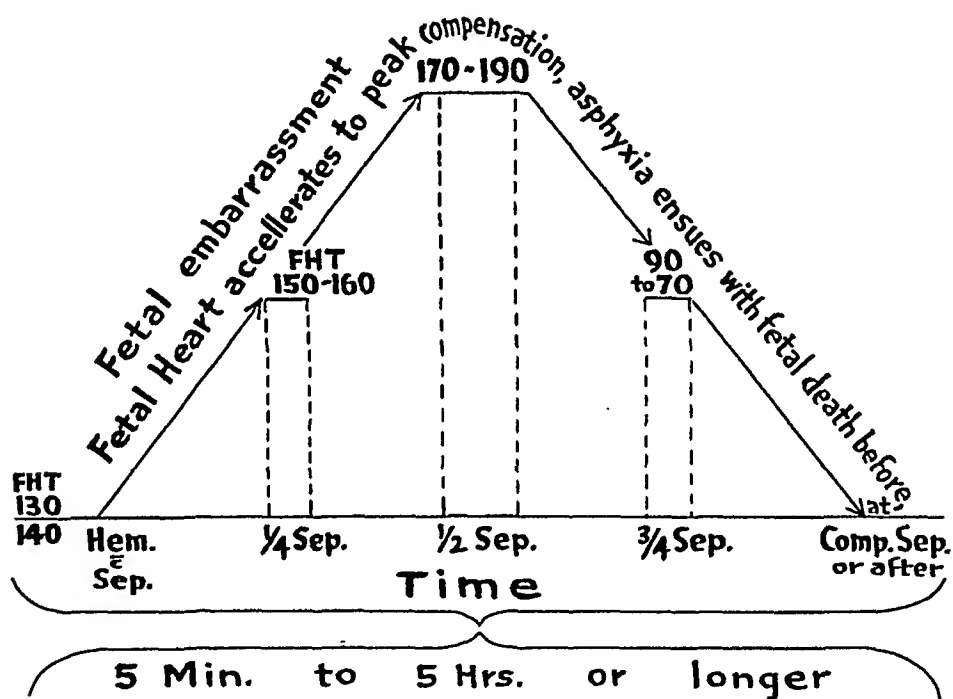


Fig. 1.

lows that with this basis one can observe the acceleration of the fetal heart rate and thereby arrive at a diagnosis of the approximate, and usually quite exact, area of placenta which has become separated. Such an evaluation renders the wide application of these figures obvious.

It must also be apparent that to secure all the information obtainable from variations in the fetal heart rate, especially in labor, the rate should be observed at definite and frequent time intervals. Such practice at fifteen- or even at thirty-minute intervals, would, in most instances, make evident the response of the fetal organism to the primary embarrassment of ablatio placenta before other signs of this complication are present, and also before this accident has reached a stage critical to mother or fetus.

Then, with an acceleration of the heart rate, instead of waiting for the appearance of external hemorrhage and instead of waiting for a ligneous hardness of the uterus, evidence of internal bleeding should be sought for as well as a failure of the uterus to relax between pains, and whether a tenderness at any circumscribed area of the uterus exists. By securing this earlier information it would be evident that, in by far the greater number of cases, ablatio placentae is not an abrupt process at all but insidious in its course and that it usually presents time for more adequate and satisfactory treatment than is usually given.

With an earnest effort toward earlier diagnosis of ablatio placentae, a conflict arises in our differential diagnosis of this condition from placenta previa, and some of the lines of difference between these two are erased. It is possible that we are even too familiar with the classical differential tables which inform us of the cessation of fetal movements in separation cases and no change in the previas, of the presence of fetal heart tones in placenta previa and their absence in ablatio.

After a study of these eight reported cases, together with two other patients who were observed and treated during the period covered by this paper, and a review of eight additional patients delivered by associates in attendance at Wesley Memorial Hospital, the writer would be inclined to disagree with certain other features characterizing the aforesaid differential tables. When ablatio placentae is recognized early, and the prerequisite of this is that the baby be watched as closely as the mother, it would appear that the onset is not as stormy nor as sudden as usually reported. None of the eight reported cases or the other two cases mentioned could be said really to have had a stormy onset.

Only one of these cases was allowed to go on to a development of a ligneous uterus. Of the cases reviewed at Wesley Hospital only three could be said to have this degree of uterine hardness. The hemorrhage naturally is visible externally at the onset of placenta previa and usually not in ablatio, although in the latter, blood would appear externally early enough to be of diagnostic aid in a reasonable number of cases. Pain has developed in these cases only on retention of a clot between the placenta and the uterus and usually in the latter part of the picture. Cases 1, 2, 3, 4, 7, and 8 had no pain, so that in these cases we were confronted with a painless and improperly called causeless hemorrhage, which is usually thought of as being characteristic only of placenta previa. The patient in Case 5 had pain attributable to separation throughout the last half of her labor. Patient in Case 6 had pain attributable to separation, the onset of the pain being three and one-half hours after the first hemorrhage and of about that duration from onset to operation.

During the three-year period which covers this series, two cases of placenta previa have come to attention where pain was a complaint of importance and in one the uterus failed to relax between labor pains. In this given interval were two cases of placenta previa where the pa-

tients entered the hospital within one hour or less after the initial hemorrhage and in which fetal heart tones were gone at the time of admission. Two patients came under observation, where on entrance to the hospital, with placenta previa totalis, sufficient separation had occurred that the fetal heart rate in the two was between 170 and 190, and in one, upon delivery of the placenta, the area of separation was estimated at slightly over one-half of the total placental area. In the other case no effort was made to identify the degree of separation.

It would seem, therefore, with the overlapping of signs and with the overlapping of symptoms in these two sister conditions, that in ablatio placentae we should start teaching the recognition of the condition on the basis of earlier findings. It would seem, further, that in recognition of these earlier findings, there is not such a wide differentiation as we are used to considering, and that one may have to rely upon the earlier bleeding of placenta previa and upon the finding, rectally or vaginally, of the placental mass, and its absence in ablatio.

It would not seem so far amiss to treat these two conditions from the standpoint of the teacher and writer, as conditions of placental separation, because after all they both come to this end eventually. It is true that the causes are anatomical in the one instance and may be intrinsic or extraneous in the other. Cognizance is also taken of the fact that in one the pregnancy started with an abnormally situated placenta, while in the other it began with a normally situated placenta. From the standpoint of signs and symptoms these conditions tie up, inasmuch as their symptom complex is almost wholly the *effect* of separation.

PROGNOSIS

In the words of Holmes,¹⁰ "Ablatio is one of the cataclysms of the child-bearing woman. Probably more is gained by a prompt diagnosis and aggressive treatment than is lost by the severity of symptoms. Procrastination is largely responsible for the maternal and fetal mortality." Various authors cite a maternal mortality which ranges from about 13 up to 50 per cent, with a fetal mortality ranging from 20 to 85 per cent. In the 8 cases reported herein and the 2, previously referred to, and in the 8 cases taken from the histories of the last 3,072 deliveries at Wesley Memorial Hospital, we have a total of 18 cases without a maternal death.

My 10 cases were distributed thus: 5 at Wesley Memorial Hospital and 5 at 4 other hospitals. In these 10 cases 7 babies were delivered alive; 3 were stillborn. Of those born alive, 5 lived, 1 died of prematurity, 1 died of asphyxia and malformations; of those born dead 1 was known to have died of toxemia before separation. The second died of a separation due to a diabetic toxemia, and a third died in utero as a result of the separation, which likewise was of toxic origin. The total infant mortality for this series is 50 per cent, the corrected mortality 30 per cent. So that when one considers that, inasmuch as most pla-

ental separations are of toxie origin, the fetal mortality must of necessity remain high. In analyzing this mortality we find that if they do not die directly of the ablatio, they succumb to the toxemia first and detachment follows, or in the one case the ablatio is productive of a premature delivery and the baby dies of the prematurity, or is indirectly a victim of the ablatio.

It is not the purpose of this paper to enter upon a discussion of treatment, further than to offer a plea of early intervention. One author advises that we must sit by the patient, watching every change; that is just what should not be done. An early diagnosis is imperative. This may be arrived at best not by simply watching the patient, but by directing earnest attention toward the fetal condition, and upon arriving at a positive diagnosis of ablatio placentae, unless delivery is imminent, resorting to immediate action. If action is taken upon the condition of the fetal heart tones and not after they are gone, if action is not deferred until the uterus is ligneous, if efforts are directed to saving the baby, the efforts in behalf of the mother will be more effectual. This is true since the earliest sign that can be observed referable to the fetus is an acceleration in fetal heart tones, which will come more often than not before the evidence of hemorrhage, and this, in turn, will be a true indication of the progress of the condition.

What action we will take must naturally be governed by the progress of labor, the condition of the cervix, and the descent of the head, but all of these in consideration of the condition of the baby as well as the mother, for anything directed toward saving the baby will be initiated earlier than if our symptom complex is based entirely upon maternal signs and symptoms.

SUMMARY

1. Placental separation disturbs the oxygen-carbon dioxide balance of the fetus.
2. This disturbed oxygen-carbon dioxide exchange accelerates the fetal heart rate.
3. The acceleration of the fetal heart rate bears a definite relationship to the area of placental detachment.
4. The fetal response is characterized by a compensatory and an asphyxia phase.
5. This response of the fetal organism presents signs which are invaluable aids in diagnosis, prognosis and treatment.
6. Earlier diagnosis narrows the differential value between ablatio placentae and placenta previa.
7. Prognosis rests on a more sound basis.
8. Treatment is facilitated by early recognition.

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30 NORTH MICHIGAN AVENUE

NOTE.—Since presenting this paper, a case has come to our attention at Wesley Memorial Hospital, in which this relation of fetal heart rate to placental separation enabled me to diagnose biovular twins before delivery.

The patient was admitted because of hemorrhage, twins were diagnosed on admission and observation of the fetal heart rates showed that the heart rate of one baby remained constant while that of the other progressively increased. The bleeding continued. It was reasoned that there must be two placentas, one of which was separating, while the other remained normally attached. Had both babies been attached to the same placenta, both heart rates would have accelerated in response to the separation. The increasing rate continued to 190, when section was performed, and two living babies were delivered. Both babies and mother survived.

DISCUSSION

DR. RUDOLPH W. HOLMES.—There have been a number of factors which have contributed to the common failure in recognition of this condition, from the beginning of time to the present day. In the order of their development they are as follows. First: Madame Boivin, one of the keenest minds in obstetric history, declared that the pregnant uterus was full, and what was full could not be more filled. She and her disciples failed to appreciate that the uterus was an elastic, distensible organ. Second: Rigby, about 1775, coined the term "accidental hemorrhage" to fit his concept that it was incident to extraneous circumstances. Third: The term *abruptio placentae* has been associated with the erroneous notion that the onset of *ablatio placentae* was always violent, sudden, explosive and such an onset is actually exceptional. Fourth: The pain is not always severe at the onset but may be extremely slight. Fifth: The *ligneous hardness*, so much emphasized, is actually mentioned in but 18 to 20 per cent of recorded cases. Dr. Richardson's contribution is of special use during the early period of the complication not only as an indicator of the fetal jeopardy and degree of separation, but also in differential diagnosis. Symptoms which are associated with other bodily dysfunctions, cerebral anemia, cardiac disease, faintness, etc., will produce no alteration of the fetal heart rate or its intensity. On the contrary, placental separation will immediately affect the character of the fetal heart.

The fetal heart acceleration, with eventual slowing due to asphyxia, is extremely frequent. At times, however, the uterine surface of the placenta will be torn during the act of separation, thus opening the fetal circulation. The resulting fetal hemorrhage will contribute to the heart acceleration, and will antagonize the slowing incident to asphyxia.

The leucocytic count is of considerable value, for in many instances of *ablatio placentae* the white count will be increased to 20,000 or even 40,000. Whether this

leucocytosis is limited to Couvellaire's uteroplacental apoplexy, or is common to all forms of ablatio placentae has yet to be proved.

DR. LOUIS RUDOLPH.—On the basis of the underlying physiologic changes, I have clinically divided ablatio placentae into the contractive and the retractive types. The contractive type is characterized by sudden abdominal pain, shock, anemia, and a ligneous uterus. The retractive type, which appears to be that of six cases in Dr. Richardson's report, has a much less acute onset, some abdominal pain, slight anemia, no shock, and a firm uterus that has a doughy consistency.

What is the physiologic explanation of the two types? In the contractive type the uterus is distended and tetanic, and no retraction of the muscle fibers related to the placental site, particularly the orbicular muscles of Ruysch, occurs. In the retractive type there is marked retraction of the musculature of the upper uterine segment and particularly the placental site or of the upper and the lower uterine segments with an arrest of the intrauterine hemorrhage.

The contractive type is safer to treat by immediate cesarean section in order to stop the hemorrhage. The retractive type can be treated in a conservative manner, because on account of the early retraction of the placental site further hemorrhage in the majority of instances will not recur.

DR. MARK GOLDSTINE.—If we follow Dr. Richardson's method carefully, the treatment of these cases should be much safer. We will save a good many more babies by watching the heart tones carefully and may prevent a rare case of rupture of the uterus.

DR. FREDERICK FALLS.—There is a difference between the case that is completely detached and the one in which the placenta is separating. Once the placenta is one-half or three-fourths detached, there is no chance for the fetus and in these cases we can turn our undivided attention to the mother. When a placenta begins to separate, no one can say how soon the separation will complete itself. What one does know is that further separation will mean death to the baby at least, and great increase in danger to the mother.

In most of these cases when the heart tones are becoming rapid or slowing to the asphyxia stage, the thing to do is to open the uterus from above and deliver the baby. Then observe the uterus and see whether there is an apoplexy at the placental site, or whether it contracts satisfactorily. If it does not contract and shows a tendency to postpartum hemorrhage, take it out. If it reacts favorably close it and leave it in.

In my clinic when a patient comes in with an ablatio placentae, the operating room is prepared as soon as the diagnosis is made. We do not always use it, but we feel that the only safe position to be in, in the presence of a uterine apoplexy, is in the abdomen where clamps can be placed on the uterine vessels if necessary.

DR. RICHARDSON (closing).—When there was early bleeding to attract our attention the fetal heart rate was constantly watched from the first sign of ablatio until the time of delivery. Early observation of the fetal heart tones in general cases did occasionally reward us by disclosing an acceleration. Whenever this occurs, one should look for internal bleeding, if external bleeding has not occurred. Every acceleration of fetal heart tones should arouse suspicion and lead us to seek other signs to confirm or rule out ablatio.

It is unfortunate that placenta previa and ablatio placentae are considered to be so different. In two cases of placenta previa which came in during the period of this investigation, the primary hemorrhage was so severe that the babies were dead on admission to the hospital, due to the amount of placental separation. In one of these conditions we have an abnormally implanted placenta and in the other a normal, but in neither are there symptoms until you have placental separation and hemorrhage. In both you may get acceleration of the fetal heart tones and in both fetal death.

SPONTANEOUS RUPTURE OF THE MEMBRANES BEFORE THE ONSET OF LABOR*

A REPORT OF 425 CASES

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DURING the six-year period from Jan. 1, 1929 to Dec. 31, 1934, there were 8,601 deliveries on the Obstetrical Service of the University of Maryland School of Medicine. Of this number, 7,045 were delivered in the home and 1,556 in the University Hospital. A number of patients referred to the hospital for delivery by other clinics and private physicians are not included in this study. These patients were practically all pathologic cases selected from the total number of cases attended by the referring clinic or physician, and it was felt that, if they were included, inaccurate conclusions would be drawn, since the normal cases from this group were not available for study. It was impossible to determine the time of rupture of the membranes in 2,132 cases, and in 57 cases the patient did not know when her pains began. The membranes ruptured and the pains began simultaneously in 140 cases. There were 304 abortions which are included in the total number of patients delivered but not included in this study because of insufficient data. The majority of the patients, who could not be included in the study because the time of rupture of the membranes or time of the onset of labor was not known, were delivered before an attendant reached the patient's home. The same is true of the abortion cases. The total number of cases discarded from the study is 2,633 or 30.61 per cent of the entire number.

Of the 5,968 remaining cases, 425 patients or 7.12 per cent had spontaneously ruptured their membranes before the onset of labor. The following study is an analysis of these 425 cases from 15 angles, namely: parity, age, race, latent period, duration of labor, relation of baby's weight to latent period, relation of baby's weight to duration of labor, relation of abnormal presentations to latent period and duration of labor, methods of delivery, cause of rupture, complications, maternal morbidity, maternal mortality, condition of babies at birth, and infant mortality during the first two weeks of life.

Parity.—Ninety-nine cases or 23.35 per cent were primigravidas and 326 or 76.65 per cent were multigravidas. These figures are very close to the ones for the entire number of patients delivered during this time, namely, 27.52 per cent primigravidas and 72.48 per cent multigravidas. As is to be expected the number of

*Read before the Baltimore Obstetrical and Gynecological Society, Feb. 14, 1936.

eases reported decreases as the parity increases, because there were fewer patients cared for who were pregnant for the tenth and eleventh times than those who were pregnant for the second and third times.

Age.—In the primigravida group, 51.51 per cent fell between the ages of fifteen and eighteen years. The youngest was fourteen years (2 cases) and the oldest forty-one years (1 case). In the multigravidas 36.8 per cent were between the ages of twenty and twenty-five years with an additional 22.08 per cent between the ages of thirty-two and thirty-five years. The youngest was seventeen years (6 cases) and the oldest forty-eight years (1 case).

Race.—There were 135 or 31.77 per cent white patients and 290 or 68.23 per cent colored patients. The total number of patients cared for during the period was 16 per cent white and 84 per cent colored. These figures seem to indicate that more white women had rupture of the membranes before the onset of labor than did colored women, but the white women are, as a rule, more intelligent and observant than the colored women, and for this reason a higher percentage of white patients may have given more complete and accurate information.

Latent Period.—There were 89 cases or 89.89 per cent of the primigravidas who had latent periods of 24 hours or less, the average period being 4.69 hours with the shortest, 0.5 hour or less for 29 cases and the longest, 23 hours for 1 case. The other 10 cases or 10.11 per cent had latent periods of 25 hours or more, the average period being 88.7 hours with the shortest 25 hours for 2 cases and the longest 336 hours for 1 case. The average latent period for all primigravidas was 13.17 hours.

Of the multigravidas 258 cases or 79.14 per cent had latent periods of 24 hours or less, the average period being 6.43 hours, with the shortest 0.5 hour or less for 38 cases and the longest 24 hours for 9 cases. Sixty-eight cases or 20.86 per cent had latent periods of 25 hours or more, the average period being 78.02 hours, with the shortest 25 hours for 1 case and the longest 672 hours for 1 case. The average latent period for all multigravidas was 21.41 hours (Table I).

Table I shows the average latent period for all cases in relation to the number of pregnancies. From a study of this table it seems that the latent periods are relatively long but fairly constant until the fifteenth pregnancy, when there is a marked sudden shortening. However, these for the most part are based upon one or two cases only, and it is impossible to draw conclusions from such a small number.

TABLE I. AVERAGE LATENT PERIOD FOR ALL CASES IN RELATION TO THE NUMBER OF PREGNANCIES

NO. OF PREGNANCIES	AVERAGE LATENT PERIOD HOURS	NO. OF PREGNANCIES	AVERAGE LATENT PERIOD HOURS
1	13.17	10	18.20
2	27.98	11	18.60
3	19.77	12	22.00
4	29.89	13	11.29
5	19.64	14	16.00
6	17.52	15	3.50
7	6.21	16	6.00
8	23.47	21	10.00
9	19.50		

Duration of Labor.—Ninety-two cases or 92.92 per cent of the primigravidas had labors of 24 hours' or less duration, the average period being 8.89 hours, with the shortest 2 hours for 5 cases and the longest 24 hours for 1 case. Seven cases or 7.08 per cent had labors of 25 hours or more, the average period being 36 hours, with the shortest 25 hours for 1 case and the longest 79 hours for 1 case. The average duration of labor for all primigravidas was 10.8 hours as compared with the accepted normal of 18 hours.

There were 316 cases or 96.93 per cent of the multigravidas who had labors of 24 hours or less duration, the average period being 7.3 hours, with the shortest 1 hour for 3 cases and the longest 23 hours for 2 cases. Ten cases or 7.07 per cent had labors of 25 hours' or more duration, the average period being 33.4 hours, with the shortest 26 hours for 1 case and the longest 50 hours for 1 case. The average duration of labor for all multigravidas was 8.1 hours as compared with the accepted normal of 12 hours (Table II).

TABLE II. AVERAGE DURATION OF LABOR IN RELATION TO THE NUMBER OF PREGNANCIES

NO. OF PREGNANCIES	AVERAGE LATENT PERIOD HOURS	NO. OF PREGNANCIES	AVERAGE LATENT PERIOD HOURS
1	10.80	10	18.00
2	7.94	11	8.00
3	6.93	12	6.00
4	8.00	13	10.14
5	8.12	14	6.00
6	8.10	15	14.00
7	7.85	16	4.00
8	8.00	21	3.00
9	16.30		

The figures in Table II indicate that one may expect the length of labor in the ninth and tenth pregnancies to be more than twice that in any other except in the thirteenth and fifteenth pregnancies where it is only slightly longer and in the sixteenth and twenty-first where it is more than $4\frac{1}{2}$ and 6 times longer. However, it must be noted that there were so few patients who had had more than 10 pregnancies that no conclusions can be drawn from these figures.

Relation of Baby's Weight to the Latent Period.—No relation of the weight of the baby to the latent period can be shown. For example, in the secundigravida group patients with 1-pound babies had an average latent period of 48 hours, with 4-pound babies almost no latent period, and with $4\frac{1}{2}$ -pound babies 31 hours. The same was found to be true in all of the other groups.

Relation of Baby's Weight to the Duration of Labor.—The only relation of the weight of the baby to the duration of labor that can be demonstrated is the one found in any group of cases; that is, large babies are frequently associated with long labors.

Relation of Abnormal Presentations to Latent Period, Duration of Labor, and Baby's Weight.—(Table III.) The average latent period for the abnormal presentation group of primigravidas was 3.5 hours as compared with 13.17 hours for the total number. Because of the abnormal presentations all deliveries were completed artificially and thus the duration of labor was shortened to a more or less degree. With one exception, the longest labors were only slightly more than the average for the primigravidas for the entire series.

Table IV for multigravidas is condensed and only averages are given to save space. However, it does show, with one exception, that the latent periods are less than for the multigravidas as a whole. The entire group had an average latent period of 21.41 hours while the longest time in the abnormal presentation series was 21.25 hours and the shortest 0.5 hour. As in the primigravidas, the duration of labor was shortened by operative deliveries. The averages in all cases, with two exceptions, compare favorably with the duration of labor for the entire group of multigravidas, that is, 8.1 hours. The one exception in the latent period was a compound presentation of head and elbow with a latent period of 120 hours. The duration of labor in this case was also prolonged, 18.5 hours. In the group of four transverse presentations there were two that had been unrecognized, and the patients

were allowed to continue in labor for some time after complete dilatation of the cervix, thus increasing the average for the group.

The size of the baby apparently had no relation to the latent period in either primigravidas or multigravidas, but as is to be expected the duration of labor does seem to increase as the weight of the baby increases.

TABLE III. RELATION OF ABNORMAL PRESENTATION TO BABY'S WEIGHT, LATENT PERIOD, AND DURATION OF LABOR. PRIMIGRAVIDAS

BABY'S WEIGHT POUNDS	POSITION	DURATION OF LABOR HOURS	LATENT PERIOD HOURS
4½	R.S.A.	2.00	7.75
5½	R.S.A.	4.50	0.50
6¼	R.O.P.	17.00	0.50
6½	L.S.A.	4.75	0.25
6½	R.O.P.	10.50	11.00
6½	L.O.P.	12.00	7.00
7¼	R.O.P.	10.75	2.50
8¼	L.S.A.	10.00	0.25

TABLE IV. RELATION OF ABNORMAL PRESENTATION TO BABY'S WEIGHT, LATENT PERIOD, AND DURATION OF LABOR. MULTIGRAVIDAS

BABY'S AVERAGE WEIGHT POUNDS	NO. OF CASES	POSITION OR PRESENTA- TION	DURATION OF LABOR HOURS	LATENT PERIOD HOURS
5½	1	Compound head-elbow	18.50	120.00
5¾	15	*Breech	10.25	18.00
6	4	L.O.P.	8.25	11.50
6½	12	R.O.P.	9.50	21.25
6¾	1	L.M.A.	4.50	0.50
8¼	4	†Transverse	15.50	8.50

*Two cases were frank breech. Others not stated.

†Actual position not stated.

Methods of Delivery.—There were 390 patients or 91.76 per cent delivered normally. There were no operative deliveries among the primigravidas that can be said to have been due to the early rupture of the bag of waters. Two operative deliveries of multigravidas were probably called for because of early rupture of the membranes. One was a case of prolapsed cord in a gravida ix delivered by version and breech extraction. The second was a neglected transverse presentation in a gravida vii delivered by decapitation. Table V shows the method of delivery for all patients with the indications for operative deliveries. Three deliveries are not noted in the table, namely, 2 cesarean sections for cephalopelvic disproportion and 1 decapitation for a neglected transverse presentation.

Possible Causes of Rupture.—A careful study was made to determine if possible any cause or causes for the rupture of the membranes before the onset of labor. There were 129 patients or 30.35 per cent who had some condition that may have caused the early rupture. However, there seems to be such a variety of causes that it is impossible to say whether one condition is more likely to cause the rupture than some other condition. From Table VI it would seem that toxemias and syphilis are in the lead, but so many more patients, among the entire number cared for during the period that this study was made, had one or the other complication or both and still began labor with unruptured membranes that one hesitates to draw such conclusions. Perhaps we may say that abnormal presentations such as breech and transverse or overdilatation of the uterus, as with twins, may have had some effect upon the early rupturing of the membranes. The fact that there were 13 sets of twins in the group would seem to confirm this impression; however, it must

TABLE V. METHODS OF DELIVERY

GRAVIDA	NORMAL LOW AND MIDFORCEPS			BREECH EXTRACTION	VERSION AND BREECH EXTRACTION
1	75	Low	2	4	0
		Uterine inertia	1	Breech pres.	
		Fetal distress	1		
		Mid	2		
		Prolonged labor	1		
		R.O.P.	1		
		Elective	15		
2	67	Low 1 R.O.P.		3	0
		Mid 1 R.O.P.		Breech pres.	
		Elective	1		
3	64	0		1	1
				Breech pres.	2nd twin trans.
4	43	Low 1 maternal dis-		1	2
		tress		Breech pres.	Trans. pres. 2
5	29	0		1	0
				Breech pres.	
6	37	0		1	0
				Breech pres.	
7	24	0		3	0
				Breech pres.	
8	20	0		1	0
				Breech pres.	
9	8	0		1	1
				Mat. distress	Prolapsed cord
10	5	0		0	0
11	5	0		0	0
12	2	0		0	0
13	6	0		0	1
					Trans. pres.
14	1	0		0	0
15	2	0		0	0
16	1	0		0	0
21	1	0		0	0

be noted that there is not one case of hydramnios in the entire series. Bicornuate and prolapsed uteri are rare enough complications of pregnancy to be considered as fairly definite causes.

Complications.—Only those complications which might have been due to the premature rupture of the membranes are listed in Table VII. The cases of infection will be discussed under morbidity. It is interesting to note that there is only one

TABLE VI. POSSIBLE CAUSES OF RUPTURE

POSSIBLE CAUSES OF RUPTURE	NO. OF CASES
Toxemias	52
Syphilis	29
Breech presentation	16
Twins	13 sets
Transverse presentation	4
Abruptio placentae	4
Low implantation of placenta	2
Prolapsed uterus	2
Syphilis and toxemia	2
Compound presentation	1
Face presentation	1
Placenta previa	1
Bicornuate uterus	1
Breech presentation, syphilis, and toxemia	1
	129

case each of prolapsed cord and arm, in spite of the fact that authorities say that the cord is very likely to become prolapsed if the membranes rupture before the presenting part has descended into the pelvis. Two patients were noted as having adherent placentas and in one case where the membranes had been ruptured for several weeks the placenta and membranes were described as being shrunken, dry, and leathery. The case of ruptured uterus was in a transverse presentation and presumably occurred because the amniotic fluid had drained away. The duration of labor in this patient was twenty-five hours, and it is reasonable to suppose that the amniotic fluid would have drained away before the time of delivery whether the membranes ruptured before or shortly after the onset of labor.

TABLE VII. COMPLICATIONS

COMPLICATIONS	NO. OF CASES
Infection	11
Uterine inertia	3
Adherent placenta	2
Prolapsed cord	1
Prolapsed arm	1
Ruptured uterus	1
Dry and leathery placenta and membranes	1

Morbidity.—Table VIII gives the corrected morbidity for the group. Those patients with definite intercurrent infections such as pneumonia, pyelitis, etc., have been excluded. A temperature of 100.4° for two consecutive days was interpreted as morbidity. Temperatures were taken twice daily on those patients delivered at home. It is quite probable that the morbidity rate would be higher if all temperatures had been taken every four hours.

There were 11 patients or 2.58 per cent in this group. Of these, 6 patients had operative deliveries which may have been the cause of the infections. Of the 5 normal deliveries, 1 patient had preeclamptic toxemia and 1 had a low implantation of the placenta. From a study of the table it appears that rupture of the membranes alone is not sufficient to cause an elevation of temperature. All patients except 1 with latent periods of 100 to 300 hours had perfectly normal puerperiums.

TABLE VIII. CORRECTED MORBIDITY IN RELATION TO LATENT PERIOD, DURATION OF LABOR AND METHOD OF DELIVERY

LATENT PERIOD HOURS	DURATION OF LABOR HOURS	METHOD OF DELIVERY	HIGHEST TEMPERATURE
1/4	3	Cesarean section	103.2°
2	7 1/2	Normal	103.0°
4 1/2	3 1/4	Normal	101.8°
5	1 1/4	Cesarean section	103.1°
11 1/2	17 1/2	Normal	101.2°
19	6	Normal	103.3°
24	24	Decapitation	102.7°
48	18 1/2	Manual rotation of head, midforceps	102.1°
60	27 1/2	Midforceps	101.4°
72	17 1/2	Normal	101.1°
120	18 1/2	Version and breech extraction	102.4°

Maternal Mortality.—The maternal mortality as far as the obstetric service is concerned was zero. There was one patient with a latent period of thirty-six hours, duration of labor four hours, and a normal delivery, who developed bronchopneumonia and died on the medical service. This gives an uncorrected mortality for the series of 0.002 per cent.

Condition of Babies at Birth.—There were 438 babies born to 425 mothers (13 sets of twins). Of this number 402 or 91.56 per cent were full-term living chil-

dren; 12 sets of twins were in this group. There were 23 full-term dead babies, but only two of these stillbirths could be said with any certainty to be due to the premature rupture of the membranes, one because of a prolapsed cord and the other a transverse presentation delivered by decapitation. Of the 12 premature living babies one set of twins may have been born prematurely because overdistention of the uterus caused the rupture of the membranes before term. There was only one premature dead baby which occurred in a case of prolapsed uterus.

Infant Mortality.—Thirteen babies or 0.03 per cent died during the first two weeks of life. The cause of death in 12 cases was given as prematurity and in 1 case the cause was not stated.

SUMMARY

1. In this series approximately 7 per cent of the patients had premature rupture of the membranes.

2. Possibly early rupture is more frequent among white than colored women.

3. The average latent period for primigravidas was 13.17 hours and for multigravidas 21.41 hours.

4. Parity apparently has no effect upon the frequency of rupture.

5. Age does not appear to play any part in the frequency of occurrence.

6. The average duration of labor is less for all patients than that generally accepted as normal.

7. The duration of labor in relation to the number of pregnancies remains almost constant except in the ninth, tenth, thirteenth, and fifteenth pregnancies, where it is approximately doubled, and in the sixteenth and twenty-first pregnancies, where it is only one-half as long.

8. There is no relation of the baby's weight to the latent period.

9. There is no relation of the baby's weight to the duration of labor that can be demonstrated to be due to the premature rupture of the membranes.

10. There is no lengthening of the latent period or the duration of labor in the abnormal presentation group.

11. The size of the baby has no relation to the latent period or the duration of labor in the abnormal presentation group.

12. Operative deliveries were not increased.

13. Toxemias and syphilis appear to cause rupture of the membranes before the onset of labor. Abnormal presentations may play some part. Twin pregnancy seems to cause early rupture of the membranes.

14. Complications are rare. The most common is infection.

15. Corrected morbidity was 0.025 per cent.

16. Corrected maternal mortality was zero.

17. There were 91.56 per cent of the babies who were born alive at full term. Only 2 dead babies can definitely be said to be the result of early rupture of the membranes, and none dying within the first two weeks of life can be attributed to this cause.

I wish to express my sincere appreciation to Dr. Louis H. Douglass for his assistance in the preparation of this paper.

CESAREAN SECTION IN DYSTOCIA

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IN PRESENTING this series of twelve cases of dystocia with dead fetus, I have divided them into two groups of six cases each.

I. In the first group there are those cases in which the presenting part has been well engaged or could be easily immobilized by an assistant, and where there has been no dangerous thinning of the lower uterine segment, marked ascent of the contraction ring, or any spastic condition of the uterus which would interfere with reduction of the size of the presenting part.

In this group there are 6 cases. There were 2 decapitations for neglected shoulder presentation, and 4 cases of craniotomy for disproportion. All 6 mothers made an uneventful recovery.

II. The second group is the one of special interest in this series of cases. Here there is no engagement of the presenting part, and it is very difficult for an assistant to immobilize it. There is marked ascent of the contraction ring and a dangerous thinning of the lower uterine segment or a spastic uterine contraction around the fetal parts.

To do a crushing operation or a reduction in the first group is relatively easy and, of course, there should be no maternal mortality directly attributable to the procedure. The second group presents a different picture. I have found it extremely difficult to reduce the size of the presenting part in this class, and the results following the attempt were so disastrous that a better solution of the problem was sought. The last 4 patients were delivered by the abdominal route, followed by hysterectomy and drainage.

This is an operation that can be performed in thirty minutes, during which time steps can be taken to overcome the condition of shock or collapse from which these patients suffer. This treatment can be carried out while the surgeon is operating, including the use of saline solution, either under the skin or intravenously, or by whatever other means one has at hand. In a few moments also the vessels that carry the blood supply can be clamped or ligated, and the source of danger from hemorrhage is overcome.

Contrast this with the long-drawn-out, destructive operation where there is more or less hemorrhage and shock to the patient throughout the entire procedure. Only recently one of the most prominent obstetricians of the country had to be carried from the delivery room, physically exhausted, after performing one of these difficult destructive operations, with delivery by the vaginal route.

The criticism may be made that we sterilize, thus preventing any further chance of childbearing under more favorable conditions. While we grant there is great force in this argument, we cannot agree that the operation should be avoided entirely on this account, for even the destructive operations with vaginal delivery may cause sterility, either from infection or the secondary operations needed to correct the resulting injuries. The decision of the method to be used should be left to the patient or her family after proper explanation has been made of the advantages and disadvantages of each procedure.

The employment of the low cesarean section in these cases may be advocated. This operation has a great value in obstetrics, and in suitable cases there can be no valid argument against its use. However, is it justifiable to leave in situ a uterus that is in all probability infected? The following are illustrations of some complications of emergency, referred obstetric cases:

In one instance, the medical attendants, relieving each other when tired, had taken several hours in futile efforts to deliver the fetus by forceps and version. In another instance the doctor spent several hours trying to anesthetize and deliver the patient by himself, alternating the use of his hands for anesthetization and his attempts at delivery. Several other cases gave a similar history of extreme probability of infection by the various maneuvers to deliver the patient. To operate by the abdominal route and leave the uterus behind, one has to disregard the conception of infection entirely. We believe operations such as cervical or low cesarean section should be limited to those cases in which the infection is only potential and not probable.

The operation of embryotomy and delivery by natural passages is not without considerable mortality, as can be seen from the following statistics: Kerr reports 10 per cent; Perry, 38 per cent; Gussman, 6 per cent; Merryweather, 8 per cent; and Shauta, 6 per cent.

In deciding upon the type of operation to be performed in any surgical emergency, one should be guided first, by the immediate operative mortality; second, by the morbidity; and third, by the probable end-result as to health and comfort. In addition in obstetric operations the possibility of future childbearing is an important factor. The extent of the procedure should in itself play no part in the decision, since, as J. Whitridge Williams once said, "What appears to be great radicalism, may prove to be the utmost conservatism."

In the Proceedings of the Royal College of Surgeons in London there is an account of a meeting held by the London Obstetrical Society in 1892 devoted solely to craniotomy. Dr. Champney, in the discussion of the merits and dangers of the operation, claimed that intrauterine craniotomy was the most dangerous of all obstetric operations. It was pointed out that these dangers were due, first, to the previous futile efforts at delivery, and second, to the great difficulty in its performance. Dr. Champney reported that of 75 patients so treated in Guy's Hospital, 4 deaths resulted from the operation, 2 deaths from rupture of the uterus, 1 death from rupture of the rectum, and 1 death from peritonitis. In a report of 106 patients treated in the Queen Charlotte Hospital, there were 9 deaths. B. C. Hirst,

in 1888, reported one death from hemorrhage. Philips, in the *British Medical Journal* (1889), reported 16 cases with no deaths, but these were not of the difficult type under discussion. While he had not performed the operation himself, Philips thought that section might be advisable under certain circumstances.

In cases of dystocia which have been neglected and poorly managed, we have performed cesarean section with hysterectomy and drainage in two types of cases, which we have designated as the "frozen" and the "balloon." In the "frozen" type, one is unable to pass one's hand any distance into the uterine cavity, because of obstruction from the contraction ring. The fetus and the uterus seem to be glued together. On insertion of the hand into the "balloon" type, there seems to be an absence of uterine walls, because of the great dilatation of the organ. One is startled by the distinctness with which one can palpate the abdominal organs. Of my 6 cases, one (Case 3) was of the "balloon" type, and the other 5 were of the "frozen" type. In the former, the shoulder of the fetus came through the uterus when the counterpressure of the abdominal wall was removed by the incision.

CASE REPORTS

CASE 1.—Mrs. K., a primipara, was admitted in 1915 to the hospital in active labor, with the history of the membranes having ruptured the day before. Her temperature was 101°, pulse 130. An abdominal examination showed a vertex presentation in an L.O.P. position, with the head floating. Fetal heart sounds were not heard. On vaginal examination the cervix was found to be about one-half dilated and the uterus tightly contracted about the fetus. It was decided that, owing to the condition of the mother and the presence of a dead fetus, a craniotomy would serve the best interests of the mother. This was attempted, but due to the difficulty of immobilizing the head, the operation was a long and tedious one with free bleeding. With continued manipulations there resulted a ruptured uterus, hemorrhage, and death of the patient on the table.

CASE 2.—Mrs. A. K., a white American-born primipara, aged twenty-six, was admitted May 11, 1917. An attempt had been made at delivery at home with the use of high forceps. The temperature was 98.6°, and the pulse 130. On physical examination the patient was found to be in a state of shock. She had a contracted pelvis with an unengaged head, and there were no fetal heart sounds. The cervix was completely dilated, the membranes ruptured, the vertex presenting. A version was done, but the head could not be pulled through. The fetus was therefore decapitated, and the head was crushed and delivered with forceps. The patient sustained an extensive tear, and on the tenth day after delivery a vesicovaginal fistula developed. This fistula on account of the late appearance was ascribable to a pressure necrosis and not to an instrumental injury at the time of delivery. After three unsuccessful attempts by several members of the staff to repair this fistula, the patient was finally made comfortable by a colpocleisis performed by William E. Parke. The lack of success in the classical procedure was due to the fact that the vesical sphincter was involved in the sloughing. A puerperal septicemia occurred, thereby slowing the convalescence. The patient was discharged on July 29, 1917, the seventy-ninth day after admission. The last report concerning this patient was in 1930, at which time she was in good general health, and retained urine in the rectum for two to three hours.

With these two disasters we were led to attempt another method of handling such cases and have adopted the abdominal route, with cesarean section, hysterectomy, and drainage. We feel it is far preferable from the results obtained with both methods. Drainage is an important part of the operation with either potential or actual infection present.

CASE 3.—Mrs. A. B., a white American primipara, was admitted to the hospital on June 2, 1921. The patient had had four previous pregnancies, the first one being a forceps delivery, after eighteen hours in labor. No adequate information could be obtained as to the other three pregnancies. The patient on admission had a temperature of 99.4° , and pulse of 115. The head was the presenting part in an L.O.P. position. Two physicians had made prolonged efforts to deliver a persistent posterior occiput, before we first saw the patient. We decided to do a cesarean section with hysterectomy and drainage. As soon as the incision was made in the abdominal wall, the shoulder of the fetus was noticed through the uterine wall. This was the type that we have designated as the "balloon" type. The patient ran an elevation in temperature from 99.2° to 102.4° for twenty-three days following operation, after which the temperature remained normal until the patient was discharged on July 13, 1921, the forty-first day after admission.

CASE 4.—Mrs. C. L., a Polish primipara, aged twenty-four years, was admitted to the hospital in active labor on Sept. 28, 1921. She had been in labor for eighteen hours, and version and forceps delivery had been attempted before admission. The physical examination on admission revealed that the patient was in a state of shock with a temperature of 100.2° , a pulse of 144, and respirations of 36. The external genitalia were edematous and bruised. The cervix was found to be completely dilated, the breech presenting, and the membranes ruptured. There was a tight band encircling the presenting part which made it impossible to reach beyond it for a foot. The uterus was tightly molded about the fetus, and the lower uterine segment felt very thin, so that it was believed any manipulation might cause it to rupture. Under ether anesthesia, a cesarean section with hysterectomy and drainage was done, using three iodoform drains. The patient made an uneventful recovery, and was discharged on Nov. 2, 1921, the thirty-sixth day after admission.

CASE 5.—Mrs. A. R., a white American multipara, aged thirty, was admitted on Nov. 16, 1921. Her first pregnancy had resulted in a three months' abortion. The pains of her present pregnancy began on Nov. 11, 1921, and were slight and irregular for five days. An unsuccessful attempt was then made to deliver her with forceps whereupon she was sent to the hospital. On physical examination it was discovered that the patient had a just minor pelvis. She was extremely pale, her temperature was 98° , and her pulse 120. The head was high and free above the pelvic brim, and the fetus was dead. Vaginal examination revealed a fully dilated cervix; the contraction ring was about the neck of the fetus and a thin lower uterine segment. It was impossible for a hand to be passed into the uterus. An abdominal cesarean section with hysterectomy and drainage was done, three iodoform drains being used. The patient's convalescence was uneventful, and she was discharged in good condition on Dec. 17, 1921, this being the thirty-first day after admission to the hospital.

CASE 6.—Mrs. E. W., a white American multipara, aged twenty-seven, was admitted on July 8, 1929. Her first pregnancy, six years previously, had resulted in an instrumental delivery. This baby was living and well at the time of her present admission. The patient had had two operations during 1927, one an appendicectomy and right salpingo-oophorectomy, and the second a plastic repair. On admission she complained of slight pains and gave a history of slight bleeding early that day, headaches, and disturbances of vision. Her feet and legs were very edematous. The

following day, since no progress had been made, medical induction of labor was tried, but failed. Next, surgical induction of labor was attempted by the introduction of bougies, which were removed twenty-four hours after insertion. Although the cervix was dilated four fingerbreaths at this time, active labor pains had subsided. Early in the morning of July 11, the doctor in attendance attempted delivery by forceps, but this also was unsuccessful. Then, internal podalic version was tried. The head was displaced from its station, and one foot and one hand were brought down. At this point the uterus became very tetanic, and Bandl's contraction ring was quite visible through the abdominal wall. It became obvious that further manipulation would probably result in rupture of the uterus. At this time I was called into consultation and the question of craniotomy or cesarean section followed by hysterectomy was discussed. While fetal movements and heart sounds were absent, it was thought that the fetus might possibly be alive, and it was therefore decided to deliver by abdominal section. The findings before operation were: Marked ascent of Bandl's contraction ring, a foot down on one side of baby's head, a hand down on the other, one was unable to pass a hand into the uterine cavity, because of contraction of the lower uterine segment, all the parts seemed to be "frozen," and head was not engaged.

A supravaginal hysterectomy was performed, and a stillborn child was delivered. Drainage was established, and the patient reacted well following the operation. Except for a slight attack of bronchitis on the fifth and sixth days after operation, the patient made an uneventful recovery, and was discharged on Aug. 5, 1929, the twenty-fifth day postpartum.

CONCLUSIONS

Embryotomy is not without danger to the mother, especially in certain types of cases. These dangers are hemorrhage, shock, rupture of the uterus, and infection.

Therefore, in cases in which craniotomy is even more difficult and hazardous than usual, I feel that cesarean section with hysterectomy and drainage offers the safest and best means of delivery, and should be performed in preference to embryotomy.

The necessity for the performance of this operation is rare, as the indications for embryotomy are fortunately becoming fewer of late years. Improved obstetric teaching and supervision in medical schools and hospitals have resulted in more adequate prenatal care, and more intelligent and careful obstetric practice. However, no problem presents greater need for good and careful judgment in its management than a dystocia which has been badly handled before consultation.

Convert, P.: Two Cases of Peritoneal Hemorrhage Resulting From Follicular Rupture, *Bull. de la Soc. d'obstet. et de Gynéc.* 25: 148, 1936.

The author reports two cases of extensive intraperitoneal hemorrhage following the rupture of an ovarian follicle. In both instances laparotomies were performed and the bleeding follicles sutured. In the discussion of this paper Cotte emphasized that in this type of case conservatism should be practiced. It is not necessary to remove the involved ovary, but only to suture the lacerated follicle. The second point brought out by Cotte is that as far as he knows there has never been a recurrence of this condition in any patient.

J. P. GREENHILL.

BRENNER TUMORS OF THE OVARY

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THIS report, based on four cases of Brenner tumors of the ovary, concerns itself with a histologic study and comments on the histogenesis. The importance of these tumors has not been stressed because of their rarity, benign character and lack of hormonal significance. Moreover, the tendency to confuse them with the folliculoid type of granulosa cell neoplasms, and their possible rôle in the etiology of pseudomucinous ovarian cysts warrant their further consideration.

The first clear picture of the histologic features of this neoplasm was presented by Orthman in 1899. It was not, however, until 1907, when Brenner described three cases under the designation of "oophoroma folliculare," that attention was directed toward the study of these tumors.

The Brenner tumors may vary in size from a minute nodule, 2 mm. in diameter, to a neoplasm as large as an adult's head. Though usually spherical or ovoid in shape they sometimes are irregularly nodular. The color is white or yellowish white, distinctly resembling a fibroma. Meyer differentiated a solid and a cystic type. The former is composed essentially of epithelial strands in a fibrous groundwork. Under magnification with the hand lens, small cavities may occasionally be discerned, varying from pinhead to cherry size, and containing an opaque, viscid, yellow brown fluid. The second and less frequent type consists of a solid Brenner tumor in the wall of a pseudomucinous or, rarely, serous cystoma.

Microscopically, the most characteristic feature is the epithelial strands which ramify in branching fashion through the connective tissue matrix. These are seen as round, oval, or longitudinal collections of an indifferent type of cell arranged in the form of pavementlike epithelium. The cells are rather large, irregular, polygonal or oval in shape with a distinct cell membrane. The cytoplasm stains faintly and appears finely granular. The nuclei are oval or slightly irregular, with distinct chromatin granules. When present, the cavitations within the epithelial nests may be only one to two cells in diameter or larger, single or multiple. The content of these cystic spaces appears often as a homogeneous, colloid material staining pink with eosin, and yellow with van Gieson. Spherical droplets of varying size and desquamated epithelium may be present. The layer of cells immediately surrounding the cavities is of particular interest. The more minute cavities may have no such differentiated layers. Some are lined by a single layer of flattened or cuboidal cells with an occasional thickening in which several layers are present. Others, however (Fig. 7), may be partially surrounded by cylindrical epithelium with basal nuclei, which shows abrupt transition into the typical indifferent type of epithelium. These cylindrical cells in many instances have been shown to take a mucicarmine stain, indicating their mucinous nature. The connective tissue between the epithelial strands is rather dense, moderately cellular and arranged in a haphazard, irregular, interlacing fashion. Areas of hyaline degeneration are usually present, and occasionally evidences of calcification are noted. The tumor as a whole is relatively avascular.

Clinically the Brenner tumors do not give rise to any symptoms or signs that are distinctive. We have been able to find 72 cases in the literature, to which 4 cases are now added. There have been two instances of bilateral ovarian involvement. Several cases have been described under other names, such as folliculoma, granulosa cell tumor, oophoroma, adenofibroma cysticum papillare ovarii, etc. An analysis of the age incidence reveals that they have been most commonly found after the menopause. Thus of the 72 cases in which the age was given, 76 per cent occurred after the fortieth year, and 60 per cent postmenopausal. The benign nature of these neoplasms is evidenced by the absence of invasive qualities, mitoses, metastases, or recurrences.

CASE REPORTS

In the four cases presented below only the pertinent clinical findings are given.

CASE 1.—A thirty-five-year-old woman was admitted to the Gynecological Service of Dr. R. T. Frank in January, 1932. She had been married for twenty years and had borne four children. The menstrual history was normal. She complained of intermittent right lower quadrant pain of several years' duration. The findings on examination suggested the presence of small uterine fibroids with diseased adnexa. A supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed.

On gross examination of the removed organs, the uterus was found to be slightly larger than normal and contained several small fibromyomas with minute areas of adenomyosis. Both fallopian tubes were thickened and bound to the ovaries and uterus. The left ovary contained an orange-sized chocolate cyst. The right ovary was irregular in shape, covered by adhesions and showed the presence of several small follicular cysts. It measured 4 by 3 by 1.75 cm. On section, a well-defined, small, yellow white, solid nodule, measuring 7 by 5 by 4 mm. was noted within the parenchyma near the hilus of the ovary. No cavities were present, grossly.

Microscopically, the organs showed multiple fibromyomatous seedlings, adenomyosis uteri, bilateral chronic salpingitis, and endometriosis of the ovaries. The nodule within the right ovary proved to be a Brenner tumor (Fig. 1). The latter was of the solid type, with 4 to 5 microscopic cavitations within the epithelial islets. The connective tissue completely surrounded the epithelial structures, was moderately cellular, and was differentiated easily from the ovarian stroma. The strands were round, oval, or irregular in shape, of varying size, and were distributed sparsely throughout the fibrous matrix. About them the connective tissue appeared compressed and more conspicuous. In one area a crescent of hyalinized tissue could be seen. The epithelial cells were round to polygonal in shape, with lightly staining cytoplasm. The nuclei were fusiform or oval in contour, with fine chromatin particles and distinct nucleoli. Near the tumor, within the hilus of the ovary, remnants of the rete ovarii could be seen, in addition to an area of endometriosis.

CASE 2.—The patient was a sixty-year-old woman who was originally admitted to the Medical Service of Dr. B. S. Oppenheimer in July, 1935 for symptoms referable to bilateral renal calculi with hydronephrosis and pyelonephritis. She had been married for thirty-eight years, had had four children and was past her menopause. In an effort to combat a mounting azotemia, a nephrostomy was performed. A general infection with *B. pyocyaneus* supervened, and the patient died on the second postoperative day. At autopsy the pelvic organs presented multiple subserous, intramural, and submucous fibroids, a right multiloculated parovarian cyst and normal tubes and left ovary. The right ovary was approximately normal in size, measuring 3 by 2 by 0.5 cm. Its surface appeared corrugated. On section



Fig. 1.—*A*, Case 1. Brenner tumor of the solid type. *B*, Higher magnification of *A*.

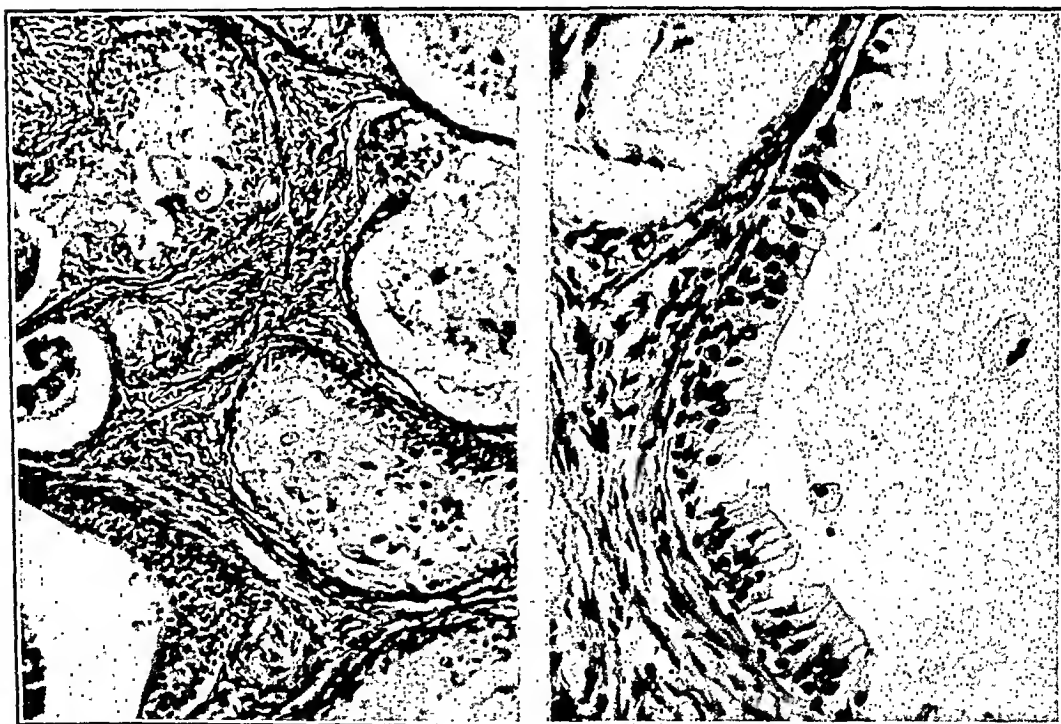


Fig. 2.

Fig. 3.

Fig. 2.—Case 2. Cavitations within the epithelial strands of a Brenner nodule. The lining consists of either a thickened layer of indifferent polygonal cells or flattened, cuboidal or cylindrical epithelium.

Fig. 3.—Case 2. High power of one of the cavities in Fig. 2, showing high cylindrical epithelium with basal nuclei. These cells and the cyst contents take a positive mucicarmine stain, indicating their mucinous nature.

several corpora albicantia were evident. Near the hilus, there was a small oval-shaped area which measured approximately 8 by 5 by 7 mm. Its outline was not sharply demarcated from the surrounding stroma, and its color only slightly more yellow white. It had a porous appearance, being studded by numerous small cystic areas varying from pinpoint to 1.0 mm. in diameter, which on section contained colloid material.

The ovarian nodule on microscopic examination was found to be a Brenner tumor. It differed from the others in that many vessels from the ovarian ligament were interspersed between the epithelial strands. The latter were numerous and for the most part cystic (Fig. 2). The contents of some of the larger cavitations included degenerating cells. A few of the cavities were lined only by indifferent cells. Others were partially or completely surrounded by a layer of cylindrical, cuboidal, or fusiform cells. In one of the more solid portions of epithelium, a radial arrangement of high cylindrical cells with basal nuclei could be seen about a central pinpoint space. With van Gieson and azocarmine stains, the condensation of fibrous tissue about the epithelial islets was especially evident. Examination with the mucicarmine stain brought out the mucinous nature of the columnar cells and the cyst contents (Fig. 3).

CASE 3.—A forty-five-year-old woman, gravida v, para iii, was admitted to the Gynecological Service of Dr. R. T. Frank in September, 1935. Her



Fig. 4.—Case 3. Hemisected ovary. The well demarcated Brenner tumor is white in color and resembles a fibroma.

menstrual history was normal aside from a four-month period of amenorrhea, immediately preceding her admission. A diagnosis of large degenerating fibroids, gravidity, and syphilis was made, and a supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed. Examination of the operative specimens confirmed the clinical diagnosis. A corpus luteum of pregnancy was found within the right ovary. The left ovary measured 4 by 2.5 by 1.25 cm. On section, between one pole and the hilus, a well demarcated, yellow white, oval-shaped nodule was found, which stood out in contrast to the grayish ovarian parenchyma about it (Fig. 4). It measured 7 by 5 by 9 mm. and appeared solid, but on serial section many minute, pinhead-sized cavities were revealed. Microscopically, the conspicuous feature of this Brenner tumor was the numerous cystic dilatations lined by flattened or cuboidal epithelium and containing pink staining, homogeneous substance. Within the narrow lamellae of connective tissue which separated these cavities, small epithelial foci were distributed (Fig. 6). One of the strands (Fig. 7) contained a cavity which was lined for the most part by large cylindrical cells with basal nuclei and sharp inner margins. At one point of its border, the cylindrical cells merged into the polygonal partially degenerated cells which made up the rest of the epithelial strand. The transition from undifferentiated cells into littoral, cylindrical epithelium seemed evident. The cysts which were so conspicuous in this case undoubtedly began as small cavitations and enlarged to finally compress the surrounding cells to a single layer of flat or cuboidal epithelium.

CASE 4.—This case was described in 1922 by Geist in a study of the histogenesis of ovarian tumors. It was classified at that time as a "tumor arising from persistent embryonal structures." The patient was a woman of fifty-two years who had complained of enlargement of the abdomen of several months' duration.



Fig. 5.—Case 3. Several of the cavitations have expanded at the expense of the epithelial structure in which they arise, leaving only a single layer of lining epithelium.

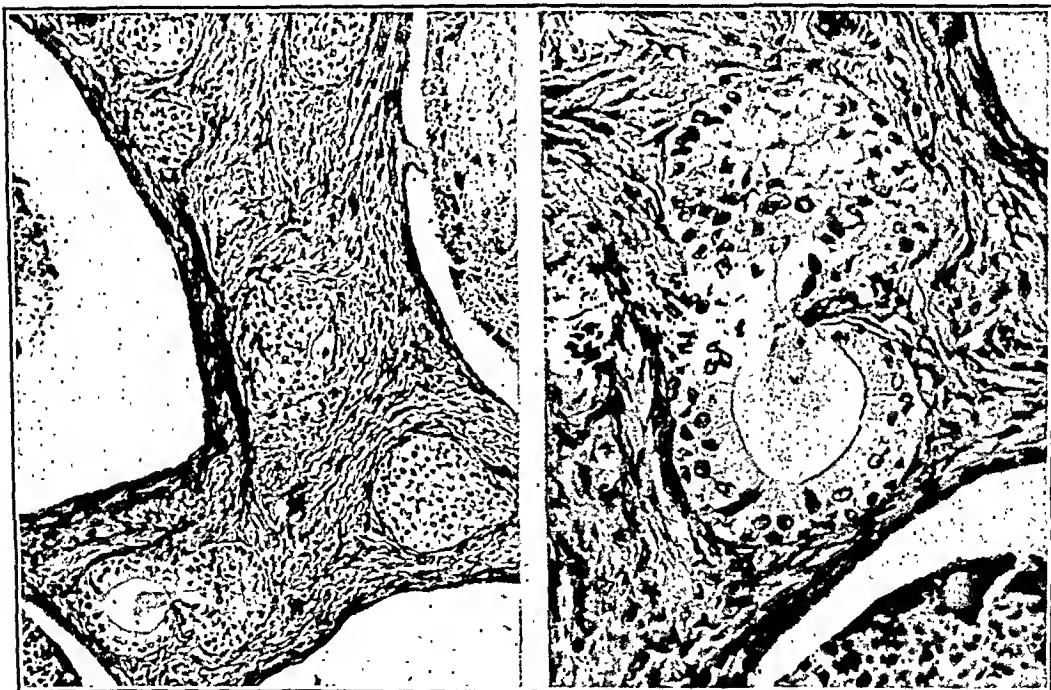


Fig. 6.

Fig. 7.

Fig. 6.—Case 3. Typical islets of pavement-like epithelial cells in a connective tissue matrix.

Fig. 7.—Case 3. Higher magnification of Fig. 6, showing the transition from indifferent to cylindrical cells.

She had never been pregnant and had not menstruated since her twenty-fifth year. Physical examination showed an abdominal mass extending to the umbilicus. A laparotomy was done and a large ovarian tumor was found. A complete hysterectomy was then performed. On gross examination it was seen that one ovary was

the site of a rather large solid tumor, apparently a cellular neoplasm, which histologically proved to be a typical adenocarcinoma. The other ovary was somewhat enlarged and contained a dense white area, 3 cm. in diameter, at one pole opposite the ovarian ligament. On reexamination this presented the typical features of a Brenner tumor. Attention was drawn at that time to the fact that in the larger cysts the lining epithelial elements were cuboidal, and in some instances approached very closely the high cylindrical cells with basal nuclei which line the loculi of pseudomucinous cysts of the ovary. It was suggested that the enlargement and coalescence of cysts within the epithelial strands, lined by a varying type of epithelium apparently transformed from the polygonal cells, could well give rise to the formation of the large pseudomucinous or serous cystomas of the ovary.

HISTOGENESIS

The occasional presence in the subserosa of the fallopian tube, mesosalpinx or ovarian ligament of isolated, epithelial foci resembling a single Brenner strand in all details has long been recognized. Though often found only on microscopic section, they may sometimes be grossly recognized on close scrutiny as minute 0.5 to 1.0 mm., white or yellowish, rather firm nodules or cysts directly beneath the serosa and movable with it. Histologically they consist of pavement-like or polygonal, closely packed cells with clear cytoplasm, deeply staining nuclei and distinct nucleoli. Finely fibrillated connective tissue surrounds them. Cystic degeneration may take place with the resultant formation of cavities, lined by either many-layered, flattened, cuboidal or cylindrical cells. The coagulated contents, often containing disintegrated cells, are analogous to those found in the cysts of Brenner tumors.

The theory that these structures are precursors of the Brenner tumor has been accepted by some authors. However, several objections have been raised: namely, the extremely rare finding of these cellular foci within the ovarian parenchyma of adults, and the failure of Brenner tumors to develop within the mesosalpinx or about the fallopian tube.

Recently Muller was able to correct the earlier impression concerning the rarity of the "paramalpighian nodules," as he terms them, within the adult ovary. In a series of 251 operative specimens, these lesions were found about the adnexa in 12 per cent of the cases. In 2.8 per cent they were discovered within the ovarian parenchyma, giving an incidence in the positive cases of 23.3 per cent for ovarian localization.

During the routine examination of an ovary removed at autopsy in the laboratories of the Mount Sinai Hospital in a sixty-three-year-old woman who died of general arteriosclerosis and cachexia, a structure was found within the cortex which consisted of a triangular area of indifferent cells adjacent to two small cysts lined by flattened or cuboidal epithelium. This on serial section proved to be a single focus. Reference to Fig. 9 illustrates the striking resemblance of its architecture to that of the tumor depicted in Fig. 5.

It is Meyer's belief that the coelomic epithelium with its unusual potentiality for abnormal differentiation gives rise in the course of embryonal development to small groups of cells within the ovarian cortex which have been termed Walthard cell nests. These indifferent cell complexes, sometimes accompanied by mucous epithelial cysts, were found by Walthard in the ovaries of the newborn and young children. The same designation has been applied to the epithelial formations beneath the serosa of the tubes and mesosalpinx. Depending upon a stimulus which is as yet unknown (hormonal and nutritional influences have been suggested), these special cell foci within the ovary may develop in several directions. If they retain their indifferent character, they may give rise to solid Brenner tumors. If the differentiation tends more in the direction of cyst formation the latter may predominate. Meyer contends that the Brenner tumor belongs genetically in the



Fig. 8.

Fig. 9.

Fig. 8.—Paramalpighian nodule occasionally found beneath the serosa of the fallopian tube, mesosalpinx or ovarian ligament. Its similarity to the epithelial strands of the Brenner tumor is evident.

Fig. 9.—A single epithelial focus with adjacent cystic dilatations found in the ovarian cortex of an adult.

series including the majority of serous cystomas, papillary cystadenomas with partial fibrosis, the adenofibromas and mixed seromucinous tumors.

Plaut holds that it is more probable that epithelial proliferation and transformation of the peritoneal lining may result in the formation of these cell nests.

Muller believes that the paramalpighian nodules of the ovary are derived from the original proliferations of the surface epithelium covering the asexual germinal gland in the early embryonal stage. Some of the indifferent cells directly beneath the surface remain dormant until under adequate stimulation they show their potentiality for bud formation. He explains the occurrence of identical cellular structures outside the ovary as follows: "The surface epithelium of the ovary and the peritoneal covering of the mesosalpinx and tube are derived from the coelomic epithelium in a single region, the 'germinal zone.' The tendency toward proliferation is not sharply limited to the coelomic epithelium covering the germinal gland

but also extends to the mesothelium immediately about it. When the latter is forced back a little later by the early tubal outline to form its peritoneal surface, it carries with it several mesothelial cells in the mesenchyme beneath it, which may under stimulation give rise to epithelial structures.''

The failure of Brenner tumors to develop within the tube or mesosalpinx cannot be adequately explained at this time. One can only speculate concerning the variations in circulation and nutrition, the question of hormonal influence, and the definitely greater propensity on the part of the ovary for tumor formation.

The histogenetic relationship of the Brenner epithelial structures to the development of pseudomucinous ovarian cysts has been mentioned. A review of the various transition stages starting with the solid strands of indifferent epithelial cells, followed by the development of cavities without a distinct lining layer of cells, and ultimately by the formation of cysts, partially surrounded by cylindrical cells having a typical pseudomucinous appearance and taking a mucicarmine stain, makes this possibility seem more likely. The final link in the chain is the large pseudomucinous cystoma with a small Brenner tumor in its wall. It is also possible that pseudomucinous cysts may develop directly from the precursors of the Brenner tumor. It is not improbable, moreover, that if all large pseudomucinous cystomas were carefully examined, small Brenner nodules might be found in their walls in a higher percentage of cases than has hitherto been reported. The frequent coincidental occurrence, however, of pseudomucinous cysts and dermoids, and the presence of small mucous cysts beneath the surface epithelium of the ovary, suggest additional etiologic possibilities.

SUMMARY

The pathologic and clinical features of Brenner tumors are described. Four cases are reported to illustrate microscopic variations. Attention is drawn to the occasional tendency to confuse this neoplasm with the folliculoma or granulosa cell tumor. The histology strongly suggests an etiologic relationship between these tumors or their precursors and pseudomucinous ovarian cysts. Careful examination of all ovarian cystomas may reveal a more frequent occurrence of Brenner nodules within their walls. The histogenesis of the Brenner tumors may on comparative histologic considerations be traced back, first, to a single epithelial focus of similar structure, termed the paramalpighian nodule or Walthard cell nest, and from there to the coelomic epithelium of the developing embryo.

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BENIGN AND MALIGNANT POLYPS OF THE CERVIX UTERI*

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CERVICAL polyps occur most frequently after the menopause, although they may appear earlier in life. The incidence of primary carcinoma of a cervical polyp is very rare judging from the literature. Among thirty-two cases seen at the Cook County Hospital Tumor Clinic, one primary carcinoma was seen. As the clinical signs do not aid in the diagnosis, microscopic examination becomes imperative.

The complete histories of the cases of mucous polyps of the cervix from the Cook County Hospital Tumor Clinic have been studied. This covers the period from January, 1932, through December, 1935. There were 2,048 gynecologic cases admitted to the clinic, of which 32 were mucous polyps of the cervix. These cases were carefully analyzed as to age incidence, parity, symptomatology, association with other lesions, microscopic diagnosis, and treatment.

COOK COUNTY HOSPITAL TUMOR CLINIC			SCHROEDER	
AGE INCIDENCE	NO.	%	NO.	%
Under 20 years	0	0.0	1	1.4
20-30 years	1	3.1	2	2.9
30-40 years	7	21.8	14	30.0
40-50 years	12	37.5	32	45.7
50-60 years	6	18.7	18	25.7
60-70 years	5	15.6	2	2.8
70-80 years	1	3.1	1	1.4
Total cases	32		70	

SUMMARY

The greatest number of patients were between the ages of forty and fifty years. Eight patients or 25 per cent were under forty years of age. Twelve or 37.5 per cent were over fifty years of age.

*Read at a meeting of the Chicago Gynecological Society, February 21, 1936.

The symptoms were leucorrhea, menorrhagia, and metrorrhagia. Fifteen or 46.8 per cent had leucorrhea, 3 or 9.3 per cent had menorrhagia, and 22 or 68.7 per cent had metrorrhagia. One patient did not have any symptoms.

The associated pathology in this group was cervicitis, prolapse, fibroids, retroversion, and cystocele. Twenty or 62.5 per cent had cervicitis, 3 or 9.3 per cent had

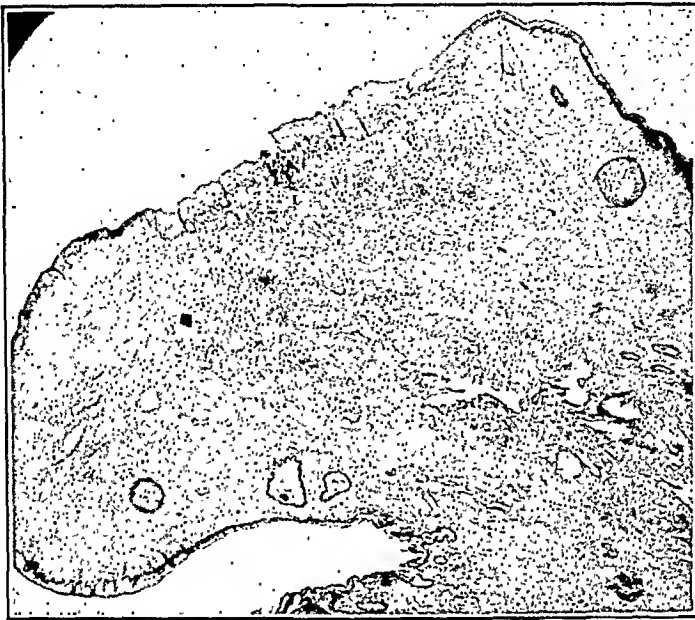


Fig. 1.—H. & E. $\times 8$. Photomicrograph of polyp arising from lower lip (portio vaginalis) of cervix uteri. The stroma is mostly fibrous and contains about six glands, four of which have undergone cystic dilatation. The polyp is covered with stratified squamous epithelium; in places there is some thickening. The base is very broad; 12×10 mm.



Fig. 2.—Case 10. H. & E. $\times 31$. Photomicrograph of benign mucous polyp of cervix uteri, composed of numerous racemose glands, lined with tall columnar mucous secreting epithelium. The stroma is fibrous. The external surface is lined with tall columnar epithelium.

an associated prolapse, 2 or 6.2 per cent had a retroverted uterus, 1 or 3.1 per cent had fibroids of the uterus, and 1 or 3.1 per cent had a cystocele. There was 1 case each of pregnancy, diabetes, syphilis, and an enlarged cystic ovary. Six patients had no associated pathology.

Of the 32 cervical polyps, 31 were definitely benign and 1 was reported as anaplastic epidermoid carcinoma. The following is the case report on Patient 14, with an anaplastic epidermoid carcinoma of a cervical polyp:

Married, white woman, aged fifty years, entered the Clinic on July 21, 1934. She was a multipara (para ii) and had had a normal menopause five years previously. The present complaint was vaginal bleeding intermittently for the last three years. In her history she states she was given local treatments about one year ago for an eroded cervix. This helped to decrease the bleeding for about eight months, but for the last four months bleeding had increased again. Vaginal examination showed a small cervix with cervicitis and a small polyp about 1½ cm. in diameter attached to the posterior lip of the cervix by a short pedicle. The polyp and pedicle felt quite firm and bled readily when manipulated. The corpus and



Fig. 3.



Fig. 4.

Fig. 3.—Case 23. H. & E. Stain $\times 210$. Photomicrograph showing racemose cervical glands of a cervical polyp exhibiting moderate metaplasia. Note conversion from tall columnar epithelium to flat squamous epithelium and some atypical overgrowth with partial filling of the gland lumen.

Fig. 4.—Case 31. H. & E. $\times 75$. Photomicrograph of mucous cervical polyp exhibiting extreme degrees of metaplasia. Notice dilated mucous glands in the left and lower portions of picture. The centrally placed glands show a transition from tall mucous secreting columnar epithelium to a flat squamous type with benign neoplasia. Some lumina are quite filled. The basement membranes are intact. There is moderate periacinar round cell infiltration, and vascular dilatation and edema of the stroma.

adnexa were negative. The polyp, including the pedicle, was removed with a Jackson square jaw biting punch forceps. The microscopic examination of a section through practically an entire cross-section of the polyp showed on one side a columnar cell covering and on the top and the opposite side stratified squamous epithelium. The uppermost area with stratified epithelium, showed marked irregularity with anaplastic proliferation, a breaking through the basement membrane and a heavy infiltration of the stroma by rapidly advancing anaplastic epidermoid malignant cells. The greater part of the right half of the section was invaded by solid malignant cell masses which invaded almost to the base of the pedicle at

the bottom. Higher magnification revealed all the typical characteristics of malignancy, including loss of polarity, hyperchromatism, mitoses, and variation in size and shape of nuclei and cells. Round cell infiltration was present in the stroma surrounding the cell masses. These masses encroached upon the racemose glands lined by the tall columnar mucous secreting epithelium. The treatment included the insertion



Fig. 5.—Case 14. Photomicrograph of the cervical polyp arising from the portio vaginalis exhibiting an anaplastic epidermoid carcinoma to the right half and at the base. H. & E. Stain $\times 36.5$.



Fig. 6.—Case 14. Photomicrograph of square area outlined in Fig. 4 ($\times 190$). Note anaplasia, and mitoses, hyperchromatism and giant malignant cells.

of 1,700 mg. element hr. of radium filtered with 2 mm. of brass into the cervical canal in three divided doses at weekly intervals, total dosage 5,100 mg. element hr. radium. At the present time there is no evidence of recurrence (seventeen months later).

COMMENT

This case is a primary carcinoma confined within a mucous polyp of the portio vaginalis. It was covered with typical squamous epithelium over the greater part of the surface. The cancer cells could be seen invading the pedicle of the polyp also.

Mucous polyps of the cervix including the pedicle should be removed and subjected to microscopic examination because of the possibility of malignant degeneration. In benign cervical polyps, removal was followed by cauterization of the cervix with the electric cautery, to prevent recurrence and to clear up the associated cervicitis. The patient should be told to watch for bleeding and vaginal discharge and to return at stated intervals for observation and follow-up. Polyps may recur or arise in other places. If the polyp is found to be a cancer, then irradiation or radical panhysterectomy is indicated.

In the cases studied, the polyps were removed and the cervix cauterized in 24 cases or 75 per cent. Vaginal hysterectomy was done in 3 cases or 9.3 per cent because of the associated prolapse of the uterus. Radium was used in five cases or 15.6 per cent.

4554 BROADWAY

DISCUSSION

DR. HENRY SCHMITZ.—Polyps may assume peculiar cell formations. It may be impossible to determine the primary origin of the cells or to render a definite diagnosis, especially with regard to malignancy. The term "metaplasia" is often applied to the reparation processes in inflamed polyps and cervixes. The use of the term metaplasia is confusing and it should be clear that the process of repair is not metaplasia.

The differential diagnosis between inflammatory hyperplasia and malignant hyperplasia should not offer any difficulty. In inflammatory hyperplasia we have a diffuse process involving a whole organ or tissue, and the cells are mature or true to type. On the other hand, in malignant hyperplasia we have a circumscribed process from an isolated group of cells, atypia of cells, and there is always penetration of the basement membrane. Long-continued irritation from various causes may terminate in inflammatory hyperplasia in the polypus and the cells may finally become atypical. We are dealing then with a transitional stage between inflammatory and malignant hyperplasia, often called precancerous. It may not be true that all precancerous stages pass on into true carcinoma, but clinical experience shows that true carcinoma follows as a rule.

DR. CHARLES E. GALLOWAY.—This subject brings up the question of early diagnosis of malignancy, especially of the cervix. We know how to diagnose a carcinoma that is as big as a pea, but the question comes up, is that of an early carcinoma. We should all try to use the microscope because in the near future early malignancy may be diagnosed by this means almost entirely. Our technicians should make better sections and tissue preparations, especially in the operating room. Tissues must be fixed properly and sectioned properly because it is under high power that the diagnosis of early carcinoma is going to be made.

Another aspect of which we know little is the time element in cases of malignancy, especially of the cervix. There is some evidence to show that tissue can resemble carcinoma and lie dormant for a period of years and still not affect the individual.

INDICATIONS FOR CONTRACEPTION FROM THE POINT OF VIEW OF THE OBSTETRICIAN AND GYNECOLOGIST*

THADDEUS L. MONTGOMERY, M.D., PHILADELPHIA, PA.

THE path of the pioneer in obstetric practice has not always been smooth. Apropos of this observation, the late Barton Cooke Hirst remarked, "We need but recall the fate of Dr. Wertt of Hamburg who in 1522 put on the dress of a woman to attend and study a case of labor, and who was burned alive for his pains; or that of Dr. Willoughby, one hundred years later, who assisted his daughter, a midwife, in a difficult labor, and was obliged to crawl into the darkened room on hands and knees."

From such statements of medical history it appears that the attempt of the curious to learn more of the secrets of maternity is not always smiled upon, nor the application of medical science to midwifery openly welcomed. Our rugged forebears are perhaps to be thanked not only for their scientific contributions but also for the fact that we are alive, and today do not conduct labor beneath a sheet, or with darkened glasses.

It is unnecessary to turn back four hundred years to note improvement in attitude of medical profession and laity toward the solution of unsettled problems. Within the memory of this author, physicians of presumably scientific inclination, gathered together to exchange views upon subjects professional, have given vent to such violence of argument that the meetings ended in the unlimbering of animosities and exchange of epithets.

The Obstetrical Society of Philadelphia, and intellectual progress in general, are to be commended that upon this second day of January, 1936, our members can meet together and discuss in quiet and unimpassioned fashion a controversial topic.

That contraception is a controversial subject of the day few will deny, for the contention between opponents and proponents wages hotly. I must confess that I am so impressed with arguments in support and points in antagonism, and so influenced by personal observation of various types of patient, that my own views on the subject are singularly unsettled. I can do little more than present to you the difficulties of decision which arise in daily practice. To this end I shall cleave to

*Read as a part of a symposium, before the Obstetrical Society of Philadelphia, January 2, 1936.

that phase of the subject which has been assigned and avoid becoming involved in the social and economic problems which are so closely related.

Two points are to be clarified before proceeding further. First, contrary to the impression which may be given by the wording of this program, the author in no way undertakes to represent in his beliefs the general opinion of the medical profession. To presume to do so would be an unwarranted assumption of authority and a failure to recognize the wide differences of opinion which exist among obstetricians and gynecologists. Second, the opinions expressed here do not represent the attitude of any department or hospital with which he is associated. The views are his own.

It is generally conceded that in the presence of tuberculosis, heart disease, chronic nephritis, previous cesarean section, and certain other subacute and chronic ailments, the occurrence of pregnancy is additional menace to the patient's health, and that some method of avoiding or limiting offspring is desirable. However, the experienced obstetrician recognizes that the universal application of such policy is a mistake, and that the establishment of rigid rules of conduct even in these more frank medical indications is impossible.

He has seen too many instances in which an arrested pulmonary infection has, under careful supervision, withstood the test of pregnancy and the puerperium, has noted many a defective heart which has tolerated several pregnancies and carried its owner to an advanced age. Even in the presence of elevated blood pressure and apparent renal impairment, he has noted patients who enjoyed a high state of health during pregnancy and were left with no added renal damage.

On the basis of these observations, the obstetrician puts aside generalities, views each of his patients as an individual problem, and has small countenance for the policy of applying contraceptive measures merely upon the name of chronic disease.

On the other hand, if he follows this method of study to its complete application, that same obstetrician will meet with other women, a survey of whose disabilities will convince him that the occurrence, the continuation, or the repetition of pregnancy is a menace to health and life. Under such circumstances it is his place to consider carefully the duty to his patient.

It is in this group of clearly defined medical indication that the arguments for contraception make their strongest appeal. What seems more in keeping with the spirit of modern medicine than to prevent or circumnavigate ill health and death? Such an argument would be unanswerable—if the present methods of contraception were uniformly successful. In those very cases where avoidance of pregnancy is most to be desired, the methods frequently fail. Perhaps the failures

which we encounter in obstetrics give us a false impression of their frequency. Perhaps those failures are the effect of human frailty and are not to be attributed to faults in the method itself. Nevertheless, I am convinced by conversation with patients and physicians that many of the present methods of contraceptive technique are esthetically distasteful, and therefore not long continued with, and that, for the lower classes at least, they are practically impossible. The net result is that contraception proves an uncertain deterrent in the most urgent of indications.

In common with a considerable body of obstetricians, I believe that where permanent avoidance of pregnancy is necessary for medical reasons, the carefully controlled operation of abdominal hysterotomy and sterilization, performed during pregnancy or at term, as the conditions may direct, is the procedure of choice. Where only temporary avoidance of pregnancy is needed, the practice of contraception has a place, and under these circumstances should become more and more useful as the methods improve in effectiveness and ease of application.

At the present time there is a growing demand to extend the field of contraceptive practice, a demand which is growing among women themselves; and not only among those who have had repeated pregnancies, but women who work and wish to avoid childbirth temporarily or permanently, young married women who desire, for economic or other reasons, to avoid childbearing during the first year or two of marital life, women who wish to fully regain health before undertaking further pregnancy, and others who wish to space their pregnancies according to a preconceived plan. All such requests reduced to their final analysis are an expression of woman-kind's desire to exercise control of her environment, to regulate a function which in the past has regulated her, to eliminate the feared and the haphazard, and substitute the welcome and the planned.

Whether such ideas are practical, scientifically founded, spiritually correct, economically sound, and socially to be sustained seems to play little part in the ever growing demand for contraceptive knowledge.

What obstetrician is not each day implored by his puerperal patients to prescribe some dependable method of avoiding pregnancy until the patient "is on her feet again," "has replenished her financial stores," or "has time to enjoy her family." He is indeed a cold individual who has no sympathy for the viewpoint of such patients, particularly those who have been under his care for many months, and who now turn to him as their confidant, advisor in health, and truest friend.

Nonmedical as many of these situations appear, the law makes little attempt to interfere with this personal relationship of patient and physician, at least in private practice, and the doctor is left to follow the dictates of his own conscience in prescribing, or withholding. Before long and before he realizes it, he is soon thrust into the position

of arbiter of childbirth, saying to this woman, thou shalt have none, to that, thou shalt have one, and to another, thou shalt have many.

I am highly of the opinion that the medical profession was never intended to assume this responsibility nor that any individual physician desires to bear it. However, since there is no other individual or board which can assume this task, and inasmuch as there appears little possibility in our present disordered existence of one being agreed upon, the physician will continue to be thrust in this unique position, to be ridiculed by some and praised by others for doing that which his conscience dictates.

It is not my place in this dissertation to go into the question of contraception as an economic panacea, or as a method of curbing the reproduction of undesirables. Already I have extended the consideration of indications far beyond the field which is acceptable to many of you. Suffice to say that sociologists and anthropologists are becoming alarmed, and not without reason, over the drifts of population growth and the failure of the more intellectual classes to reproduce themselves. These same authorities condemn the practice of contraception as an instrument of still further class imbalance, finding the method unsuccessful where most needed and too successful where least indicated.

The implications of these findings, while not of direct bearing upon the science of medicine, are of interest and importance to any group of scientific men. This subject is too large to enter upon at this time, but there is one observation that I wish to leave with you. The people of the United States are not easily brought under prohibitions, as witness our recent experience with the liquor traffic; they, like all people however, are susceptible to suggestion. Instead of expending our energies upon the legal restriction of contraceptive practices, would it not be more effective, and is the time not ripe for a carefully laid campaign of propaganda setting forth the permanent joys of motherhood, the lasting pleasures of family life and of children, designed to encourage further reproduction by creating greater deductions in income tax and by making grants to worthy families? *Many would be led who cannot be driven.*

If there are any conclusions to be reached from this rambling discourse, they may be set down as follows:

1. The present technic of contraception is an unesthetic, unreliable method of avoiding pregnancy. Its successful practice should be limited to temporary ailments.

2. Under indications of a serious and permanent nature, such procedures as hysterotomy and sterilization are more dependable and are to be preferred.

3. A demand for the extension of contraceptive practices is growing among the female population and breaking all bonds of church and state.

4. There is a disposition at present to leave this problem, in the case of the individual patient, in the hands of the obstetrician, placing him in a unique and difficult position.

5. Certain socially minded and economically concerned groups propose contraception as a panacea for the problem of the poor. This proposal calls for critical inspection on the part of scientific men, and the physician should take appropriate interest in the correct solution.

6. Too much is expected of the practice of contraception as an instrument of racial betterment. Properly conducted propaganda designed to elevate the position of motherhood and extol the pleasures of family life will do more to increase reproduction in the upper classes.

1930 CHESTNUT STREET.

NOTES ON THE USE OF THE RECENTLY INTRODUCED ERGOT ALKALOIDS IN THE PUERPERIUM

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THIS report adds an additional 218 cases in which ergotamine tartrate was administered in the puerperium, bringing the total to 618 so treated, and 116 who were given "ergoklonin," a liquid preparation of ergot claimed to contain the ergostetrine of Thompson. Ergostetrine, the active principle of "ergoklonin," is apparently identical with the ergometrine of Dudley and Moir. Although 33 other parturients were given ergotrate (the ergotocin of Kharasch, Legault, Davis and Adair), the number so treated is too small from which to draw any definite conclusions.

Ergotocin is marketed in tablet form, each tablet containing 1/320 gr. of the alkaloid. The dose employed in our series was 1/640 gr., repeated four times daily, for three successive days. Unfortunately, ergotocin is not stable in solution, so that its use as a puerperal prophylactic, other than the immediate control of bleeding, is precluded. It does seem reasonable to say, that when ergotocin can be had in stable solution or in smaller tablets, we may have a satisfactory puerperal, prophylactic agent.

The use of the various ergot alkaloids here described is primarily to obtain tonic contraction of the uterus, the early emptying of the uterine canal, the inhibition of the propagation of saprophytes, and the control of puerperal morbidity rather than to control postpartal hemorrhage. It is not the speed of action nor the intensity that is desired, although these are commendable attributes, but the persistence and tonicity produced and maintained. This is why the individual dose used has always been less than the one customarily prescribed.

ERGOTAMINE TARTRATE

As heretofore, 1 e.e. of ergotamine tartrate was administered, hypodermically, immediately after the expulsion of the placenta, and thereafter, 6 minims every four hours for 5 doses daily on the ensuing three days, orally. Among the 218 so treated, there were 95 primiparous and 123 multiparous women, including three sets of twins. 190 were in the occipitoanterior and 17 in the occipitoposterior position. There were 9 breech, 1 transverse, 1 brow, and in 3 the position was undetermined. Six infants were delivered with low forceps and 5 with midforceps. There were

one version and extraction, one breech extraction, and one bag induction. The placenta was removed manually twice. The operative incidence rose to 8.5 per cent. Approximately 29 per cent of the babies weighed between 3600 and 5400 gm.

Involution.—Again in this series as in the larger group, the uniformly small size of the uterus was quite apparent. The average height on first day was 12.62 cm., the extremes were 6 and 17 cm. Thereafter involution progressed steadily. On the tenth day the average height of the fundus of the uterus was a little over 1.8 cm. (Fig. 1).

Lochia.—In no case was the lochia noted as being profuse in amount, while in 3 it was absent. In 147 or 67 per cent it was moderate in quantity while in 30

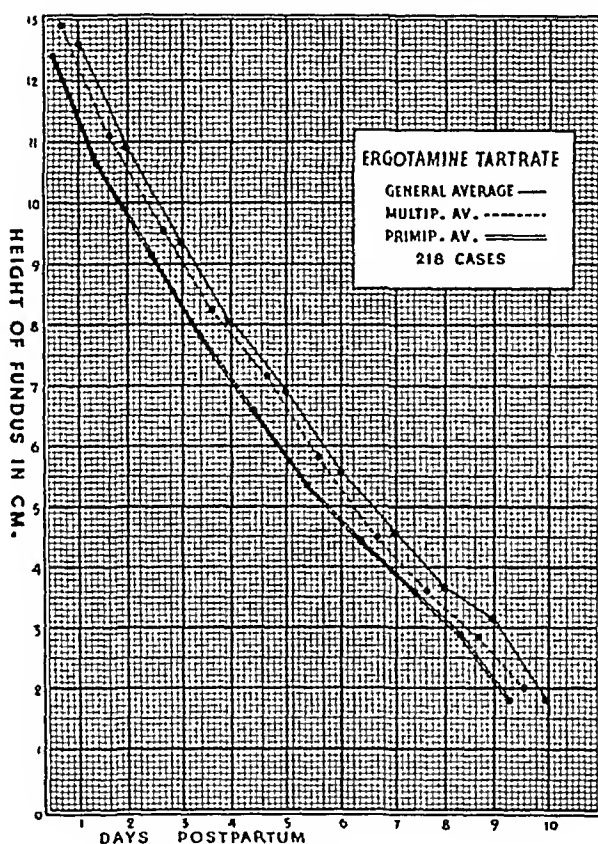


Fig. 1.

per cent it was scant. The character of the lochia followed a similar parallel. In 61 or 28 per cent it was noted as rubra. In 129 or 59 per cent it was serous, while in 26 or 12 per cent it was colorless.

In 6 cases or 2.7 per cent the lochia was foul. It is not unreasonable to suppose that the fertile soil so necessary for the development of the saprophyte is reduced to an absolute minimum. A 28 per cent lochia rubra, likewise, shows a fair control of the bleeding elements.

Temperature.—With involution progressing satisfactorily, and an absence of saprophytic invasion, it should follow, barring any nonobstetric infection, that few, if any parturients should have any fever. We have again elected to use the same three standards as heretofore, the American, British, and DeLee's. Our uncorrected morbidity rose slightly, but the operative incidence had also risen. Among the 10 febrile patients, there were one with bilateral hydronephrosis and hydroureters, one with acute cystitis, two with acute mastitis, three with sapremia, and three with acute endometritis, one of whom had an infected, episiotomy wound.

If we subtract the first four cases, the corrected morbidity is 2.75 per cent.

ERGOKLONIN

For some reason, we have not had the success with ergoklonin that we had hoped. One hundred and sixteen parturients were given this alkaloid. They received two drachms immediately upon the delivery of the placenta and one-half drachm four times daily, on the succeeding three days.

There were 118 babies born, including two sets of twins: 104 were in occipito-anterior position; 6, occipitoposterior; 5, breech; and in 3, the position was undetermined.

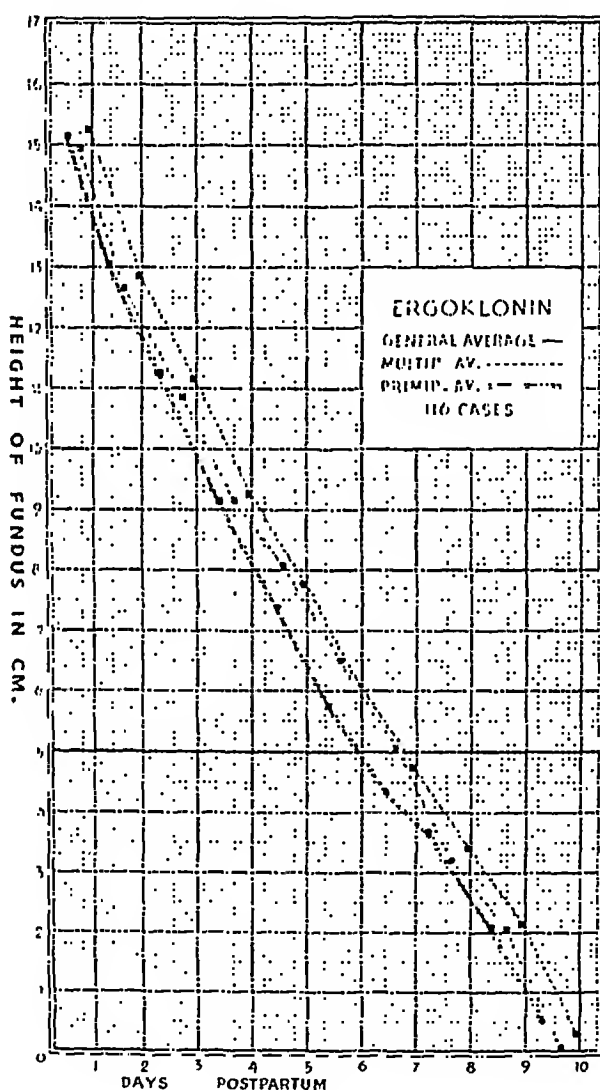


Fig. 2.

The operative incidence was 8.6 per cent, 6 were delivered with low forceps, one midforceps, one axis traction, and one had a bag induction.

Over 29 per cent of the babies weighed more than 3600 gm. (Table I).

Involution.—Involution proceeded quite satisfactorily. By the tenth day the fundus of the uterus was just palpable behind the symphysis pubis (Fig. 2). The greatest comparative discrepancy was in the first few days of the puerperium. The average involution for the first day was 2.5 cm. The ergoklonin must be credited with this marked contractile power, inasmuch as neither in the ergotamine tartrate group nor in the few cases receiving ergotrate did there appear so marked a first-day involution.

TABLE I. BIRTH WEIGHT

WEIGHT IN GM.	ERGOTAMINE TARTRATE PER CENT	ERGOKLONIN PER CENT
Under 2,250	1.6	5.3
2,250-3,600	69.13	65.48
3,600-4,050	19.42	22.12
4,050-4,500	8.57	7.08
4,500-5,400	1.00	

TABLE II. MORBIDITY IN 218 CASES

AMERICAN STANDARD*		BRITISH MED. ASSOCIATION ADDITIONAL		DE LEE STANDARD				TOTAL	
				FIRST DAY ONLY ADDITIONAL		ONE DAY OTHER THAN FIRST ADDITIONAL			
NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
10	4.5	3	1.83	10	4.5	29	13.3	52	24.1

*Corrected morbidity according to American standard was 2.75 per cent.

However, a new factor made its appearance. Over 65 per cent of these women had pain, varying in intensity from mild to severe, and limited to the duration of the administration of ergoklonin. All this would seem to imply that the dose, one-half drachm, four times daily, was too large. Further evidence of perhaps a too tonically contracted uterus appeared in the lochia.

Lochia.—At the time of discharge from the hospital, the lochia was moderate in 87 or 75 per cent, scant in 16.5 per cent and absent in 7 per cent. It was colorless in 5.8 per cent, serous in 58.5 per cent and red in 26.5 per cent. That a too forceful contraction was being obtained was apparent by the unusual number of foul lochia discharges, 26 or 22.4 per cent. Within a short while after the cessation of the administration of this alkaloid the foul lochias cleared.

Temperature.—Among the 12 febrile patients, there was one with pyelitis, one with an ischio-rectal abscess, one had had a postpartum hemorrhage, one with an infected episiotomy wound, six with sapremia, and two with acute endometritis. This is an uncorrected morbidity of over 10 per cent. If the first two are eliminated the morbidity is still high, 8.5 per cent. It is noteworthy that the sapremias make up 60 per cent of the morbidity.

TABLE III. ERGOKLONIN MORBIDITY

AMERICAN STANDARD*		B. M. A. STANDARD ADDITIONAL		DE LEE STANDARD				TOTAL	
				FIRST DAY ONLY ADDITIONAL		ONE DAY OTHER THAN FIRST ADDITIONAL			
NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
12	10.34	4	3.44	5	4.31	19	16.4	40	34.49

*Corrected morbidity according to the American standard was 8.5%.

To those of us who watched these patients from day to day, it was apparent that the too tonic action of this oxytocic accounted for the large number of sapremic temperatures. It does appear, however, that in smaller amounts in like or at greater intervals far better results may be obtained.

DISCUSSION

The administration of ergotamine tartrate in over 200 patients in the current series fully substantiates our previous findings.¹ That the morbidity rose only 0.5 per cent, despite a doubled operative incidence, from 4.25 per cent to 8.5 per cent, lends strong support to the feeling that a suitable oxytocic should be used in the lying-in period. The absence of pain and foul lochia in these patients bespeaks the absence of undue tonic contractions of the uterus.

Regrettably, the results with ergoklonin were not as satisfactory. Although the involution of the uterus was all that could be desired, too many had two annoying symptoms, pain and foul lochia.

Our experience with ergotrate (ergotocin) is quite meager, being limited to a few more than 30 patients. These showed an equally rapid involution, a larger percentage of scanty lochial discharge, 26 out of 33, and only one had a foul lochia.

Dr. DeLee² in a personal communication, writes, "Many years ago, over forty, my preceptor used to give ergot regularly, after every delivery. However, with the improvement of our methods of asepsis, we found it was not necessary and gave it up.

"Latterly, with the increase of the dangers of infection incident to childbirth in general hospitals, where the maternity wards are not as well isolated as they might be, perhaps we ought to resume this ancient practice."

With the essence of this I wholeheartedly agree. However, we cannot fail to note that our morbidity rose only one-half of 1 per cent, while the operative incidence increased 100 per cent.

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901 WASHINGTON AVENUE.

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The ketogenic diet treatment of urinary infections introduced by Clark and Helmholtz has proved efficacious. Its bacteriostatic power is convincing, but a practical difficulty arises in carrying it out. It entails rigid skilled dietetic supervision, is nauseating and expensive. It owes its bacteriostatic power to the presence of β -hydroxybutyric acid in the urine of patients under a ketogenic diet treatment. No effect is produced on urinary infection by the oral administration of this acid, since it becomes completely oxidized before reaching the urine.

Attempts have been made to find a nontoxic acid which would exert a similar bacteriostatic effect but which would not be oxidized when given orally and which would be excreted unchanged in the urine. Rosenheim claims mandelic acid fulfills these requirements. He administered 12 gm. daily in divided doses. The urine is rendered strongly acid by ammonium chloride gr. 10 \times 6. It forms an effective substitute for the ketogenic diet treatment.

The author reports 16 cases in 13 of which the treatment was successful in sterilizing the urine fairly rapidly. The series comprised male and female patients having diverse organisms and chronic infections of the urinary tract. This treatment is contraindicated in patients showing renal impairment due to the deleterious effects of acids on the kidney function in such individuals. In all other cases of severe chronic urinary infections it is a simple and practical therapeutic advance.

F. L. ADAIR AND S. A. PEARL.

PREMATURE SEPARATION OF THE PLACENTA

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ACCIDENTAL uterine hemorrhage of Rigby,¹ or ablatio placentae of Holmes,² or abruptio placentae of DeLee³ is defined in the standard textbooks of obstetrics⁴⁻⁹ as uterine hemorrhage from a premature separation of a normally implanted placenta. The case reported and other experiences of the author have suggested that this condition should be defined as uterine hemorrhage from a premature separation of the placenta, irrespective of its attachment to either the upper or the lower uterine segment. On the basis of the underlying pathologic and the physiologic changes, I suggest a clinical classification of the contractive and the retractive types.

CASE REPORT

Mrs. J. B., aged twenty-six years, colored, gravida x, and para vii. The family and personal history were of no importance. The patient had had no prenatal care. The last menstrual period was probably in February, 1934. The patient was admitted to the Obstetrical Service of the Cook County Hospital on Sept. 30, 1934, at 1:25 P.M., on account of a sudden sharp abdominal pain lasting for about five minutes which was followed by a moderate degree of vaginal bleeding that occurred at 10 A.M. A moderate degree of vaginal bleeding was present when the patient was admitted to the hospital. The patient had felt fetal movements the evening before, but no fetal movements since 10 A.M. She had been in good health until the above attack.

Physical Examination.—A well-nourished, obese, and well-developed colored female who did not appear ill. Temperature 98°, pulse 72, and respirations 18. Blood pressure 185/130. The uterus was the size of a full-term pregnancy, firm, and yet of a doughy consistency, and not tender. The fetus could not be palpated. No fetal heart tones could be heard. The maternal pulse was regular and of good quality. No signs or symptoms of hemorrhage or shock.

Vaginal Examination.—The cervix was lacerated; the cervical canal admitted one finger; no effacement, but evidence of blood in the cervical canal. The bag of waters was intact through which the fetal head could be palpated, although the station of the presenting part was minus four. No placental tissue palpable.

Laboratory Findings.—Urine: Albumin was plus three with negative microscopic findings. Sugar was negative. Albumin was negative from October 7 to the date of the patient's discharge from the hospital. On October 12, twenty to thirty white blood cells were found per field under low power. The Kahn test was negative. White blood count was 17,500 per c.c. on October 9. Vaginal smear was positive for the gonococcus.

Diagnosis.—Cephalic presentation, revealed accidental hemorrhage of the retractive type. Dead fetus.

Treatment.—A laparotomy was performed at 7:30 P.M. under ether anesthesia. The abdomen was opened by a median infraumbilical incision. The uterus was

apparently at term, firm, although doughy. Throughout the uterus were seen irregular purplish streaks. The uterus was twisted about 40 degrees to the left. A moderate amount of a serous exudate was present in the abdominal cavity. The torsion of the uterus was easily corrected, and it was incised in the midline high on the anterior uterine wall. No bleeding was present; and the walls were markedly thickened to about 4 cm., which thickness extended down to the uterovesical junction. The uterine cavity presented clotted blood, but no evidence of fresh blood.

The fetus was delivered by breech extraction. The umbilicus was clamped and cut. It was observed that the uterus did not contract and retract as is usually seen during the performance of cesarean section. The hysterotomy wound was immediately brought together and clamped with a few Allis forceps. A routine supravaginal hysterectomy was performed.



Fig. 1.—The specimen was bisected on the posterior uterine wall. I is the left posterior uterine wall, II is the right posterior uterine wall. On the left side is noted the fully attached placenta. On the right side the placenta is completely detached from the uterine wall with clotted blood between it and the uterine wall. AB is the section removed from the left posterior uterine wall for histologic examination.

Pathology.—The specimen was immediately fixed in Kaiserling's solution, and later in a formalin solution. The specimen is a supravaginal amputated gravid uterus, measuring 15 by 14 by 9 cm. On the anterior surface near the right border, there was an incision measuring 90 mm. in length. The edges were gaping and slanting downward. The greatest thickness of the uterine wall was found at the placental site which measured 53 mm. The serosa of the formalin fixed specimen was gray with many hemorrhagic areas. Many ragged pieces of a white membrane and of a brown hemorrhagic tissue were protruding from the endometrial cavity. The placenta was attached mainly to the anterior uterine wall and extended on the left side to the posterior uterine wall. The placenta was attached to the left upper and lower portion of the uterus. It was separated from the right upper and

lower portion of the uterus on the anterior and posterior uterine walls. Many blood clots were present between the detached placenta and the uterine wall. The location of the placenta was that of a placenta previa marginalis (Fig. 1).

Histologic Examination.—A section was removed from the left lower portion of the posterior uterine wall and its attached placenta to determine whether the placenta was attached or had slipped down from the upper uterine segment. It showed the placenta attached to the left lower portion of the posterior uterine wall.

The postoperative course was uneventful, except for a moderate degree of temperature until October 21. The abdomen was normal throughout. The temperature appeared to be due to a mild pyelitis. The patient was discharged from the hospital on the twenty-eight postoperative day.

The case reported from an anatomic standpoint demonstrates a placenta previa marginalis and an accidental uterine hemorrhage of the Couvelaire type. The author has had a number of experiences with accidental uterine hemorrhage in which cesarean section, with and without hysterectomy, was the indication in which it appeared that the placenta was probably attached in part to the lower uterine segment, but on account of the rapid separation of the placenta this feature could not be anatomically demonstrated.

The history and the clinical signs and symptoms led to the diagnosis of accidental uterine hemorrhage, although placenta previa lateralis was seriously considered. The outstanding feature in this case is the normal pulse and the abdominal findings which have been a common observation; the abnormal degree of thickening of the upper and the lower uterine segments in spite of the fact that labor had not, as yet, set in and the cervix had not undergone any degree of effacement or dilatation.

The literature characterizes the consistency of the uterus as ligneous or boardlike in accidental uterine hemorrhage. I have seen a sufficient number of these cases in which the consistency of the uterus could not be described as being ligneous. The clinical course of this type of obstetric complication has led me to adopt the classification of the contractive and the retractive types which is based on the underlying physiologic uterine changes.

The contractive type is characterized by a sudden onset of abdominal pain with early signs and symptoms of shock, evidence of marked and progressive anemia, and a ligneous uterus. On exploration the uterus is found in a marked tetanic state or ligneous uterine walls thickened to about 2 cm., and intrauterine examination discloses the presence of dark clotted and fresh blood. During the hysterotomy incision the uterine walls bleed freely. The physiologic sequence consists of a sudden abruption of the placenta from its attachment, complete or partial, and a compensatory contraction with a slight degree of retraction in the attempt to arrest bleeding from the placental site. The uterus remains in a state of isometric contraction, but owing to insufficient retraction of the placental site the maternal sinuses remain open, which permits bleeding into the uterine cavity to continue. This bleeding

continues until sufficient blood has flowed into the uterine cavity to lower the general vascular pressure. When the intrauterine pressure equals the lowered general vascular pressure, the uterine hemorrhage is arrested, but the patient is severely bled out. The shock is due to the trauma induced by the uterine tetany plus the distention of the uterus by the intrauterine hemorrhage; and if a toxemia of pregnancy is present, this constitutional state and the continued intrauterine bleeding cause a gradually increasing state of shock.

The retractive type is characterized by a more or less sudden onset of abdominal pain; the uterus may enlarge somewhat, is firm but of a doughy consistency; the anemia may be slight or absent, but there is no evidence of shock. The pulse is usually of normal or slightly increased rate and of good quality. With a slight revealed uterine bleeding, the differential diagnosis is between placenta previa and accidental uterine hemorrhage. The physiologic sequence consists of a more or less sudden abrupture of the placenta from its attachment, complete or partial, followed by a rapid and marked retraction of the upper and the lower uterine segments in the attempt to arrest the bleeding from the placental site. After a varying degree of intrauterine bleeding the placental site undergoes sufficient retraction to completely close the maternal sinuses and arrest the bleeding; and then the uterus remains in a state of isometric contraction.

Retraction is a physiologic phenomenon found only in the uterus during parturition. It consists of a certain degree of permanent shortening of the muscle fibers of the upper uterine segment during a uterine contraction.¹⁰ Duncan¹¹ stated that retraction is the specific property of the uterine musculature, and is independent of the phase of a uterine contraction. In elective cesarean section, before the onset of labor, we know that retraction manifests itself in the upper uterine segment immediately as the fetus is being extracted. We note during the incision of the upper uterine segment that bleeding from the uterine wall is quite active, but as soon as the fetus is extracted, the uterine walls thicken and the bleeding is more or less arrested, which phenomenon is due to the property of retraction. In the dog the rate of retraction of the ampullae is governed wholly by the rate in which the fetus is removed. That is, in the dog not yet in labor, if a laparotomy is performed and by hysterotomy a fetus is removed from an ampullae, the retraction immediately takes place. On the basis of clinical experience with the human being and clinical and experimental experience with labor in the lower animals, I am of the opinion that the physiology of the retraction of the uterine musculature is independent of the phase of contraction of a uterine contraction. During labor the physiology of the uterus relative to the phases of contraction and retraction is usually coordinated. In uterine dysfunction the upper

and lower uterine segments may undergo abnormal synchronous retraction which will lead to a functional dystocia, but rupture of the uterus will not result.

The normal retraction of the uterus takes place during the first stage of labor and is manifested in the upper uterine segment, while the lower uterine segment undergoes some stretching or thinning which is referred to as the law of polarity. During the second stage of the labor the upper uterine segment undergoes further retraction or thickening while the lower uterine segment holds or undergoes some slight stretching or thinning until the ovoid is expelled. During the third stage of labor, we have the following changes: Immediately after the expulsion of the ovoid the uterus may temporarily relax with an arrest in the mechanism of placental separation, or, immediately with the expulsion of the ovoid the upper uterine segment undergoes excessive contraction and retraction, particularly the placental site, which is demonstrated during the performance of cesarean section with the result that the chorionic villi are separated from the placental site, followed by the formation of a retroplacental hematoma which aids in the separation of the placenta from the placental site. After the placental separation the upper uterine segment undergoes further contraction and retraction, and with a synchronous contraction of the lower uterine segment, with or without the aid of intraabdominal pressure, the placenta is expelled from the uterovaginal canal. After the expulsion of the placenta the placental site undergoes excessive retraction which keeps the maternal sinuses closed and so permits thrombosis and organization to take place. The lower uterine segment immediately after the placental expulsion is usually found in a flaccid state, but the upper uterine segment maintains its state of retraction.

In the above instances the law of polarity may be disturbed by a temporary contraction of a transverse segment of the uterus with an incoordination of the uterus above and below the zone of constriction as is seen in cases of constriction ring dystocia.¹² In the retractive type of accidental uterine hemorrhage, we may find retraction taking place only in the upper uterine segment, particularly at the placental site; or it may involve synchronously the upper and lower uterine segments as is demonstrated in the reported case. The clinical importance of this pathologic physiology of the uterus during pregnancy and labor will be demonstrated in a paper on the lower uterine segment.

The case reported brings up a very important etiologic factor as to what brought about the acute onset, the accidental uterine hemorrhage or the placenta previa. The specimen shows a uteroplacental apoplexy of Couvelaire and a partial separation of the placenta from the upper and lower uterine segments. It is seen that the placenta is mainly separated from the right upper and lower portion of the uterus. The station of the presenting part was minus four or high which in itself

speaks for a placenta previa, because I have observed for many years that in placenta previa the station of the presenting part is always high at the onset of the bleeding. I have never found the presenting part low in the pelvic cavity in cases of placenta previa.

The lower uterine segment is gradually elongated during pregnancy, and during the last month of pregnancy there is either a gradual or a sudden abrupt elongation of the lower uterine segment which is known as the phenomenon of "lightening" or the final physiologic phase of the preparation of the uterus for parturition.¹³ During any phase of the elongation of the lower uterine segment the solid placenta in part is separated from the lower uterine segment which is the mechanism of bleeding in placenta previa. I believe that in this case the "toxemia of pregnancy" was of a chronic form and the placenta previa was the active cause of the onset of the signs and symptoms and was followed by a premature separation of the placenta from the right upper portion of the uterus. Yet, in retrospect with the clinical and pathologic findings I am inclined to believe that the diagnosis should be placenta previa marginalis complicated by a chronic form of accidental uterine hemorrhage.

The classification of accidental uterine hemorrhage in the contractive and retractive types is of clinical value in the diagnosis and management. In the contractive type, on account of the underlying physiologic changes, the indication must be of a radical nature in order to empty the uterus of its contents in order to combat the hemorrhage and shock. Cesarean section, with or without hysterectomy is the safest treatment for the patient. When the choice of delivery is per vaginam, and the patient is in the first stage of labor, the bag and the Spanish windlass are indicated. Before the bag is inserted some of the liquor amnii and blood should be allowed to escape in order to somewhat decrease the intrauterine tension which will permit the uterus to relax, therefore favoring contraction and retraction to overcome the state of isometric contraction which has prevented the contraction and retraction of the uterus for the mechanism of the expulsion of its contents.

The retractive type, on account of the underlying physiologic changes, may be conservatively treated in emptying the uterus of its contents. This is particularly important in a primipara. After the primary hemorrhage, the early retraction of the upper uterine segment, and particularly the placental site, brings about an arrest of further hemorrhage from the placental site. These cases can be treated with intelligent expectancy until an indication arises for radical treatment. If the patient is not in labor, then labor may be induced by medical or operative measures. It is a frequent occurrence in normal labors that with the expulsion of the placenta, we find evidence of clotted blood attached to the maternal surface of the placenta which makes us consider the possibility of a mild accidental uterine hemorrhage having been pres-

ent, but since we have had no revealed bleeding, we must consider the premise that the separated portion of the placental site was closed by retraction during the labor.

SUMMARY

In view of the case reported with the anatomic evidence of accidental uterine hemorrhage and placenta previa marginalis being present in the reported case warrants the suggestion that the definition of this obstetric complication should be changed. The definition as is accepted makes it *specific* that the placenta must be situated above the physiologic retraction ring or on the upper uterine segment before its separation. In view of the above considerations I would suggest that accidental uterine hemorrhage should be defined as a *premature separation of the placenta*. On the basis of the physiologic changes underlying the clinical course, the author suggests the clinical designation of accidental uterine hemorrhage as of the contractive and the retractive types.

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Wolfe, Samuel A., and Kaminester, Sanford: Granulosa Cell Tumor of Ovary, Am. J. Surg. 31: 471, 1936.

Granulosa cell tumors of the ovary have been erroneously interpreted as atypical carcinomas, sarcomas and endotheliomas. Solid, cystic and combined forms of the neoplasm occur. The yellow color is indicative on gross examination. The histologic appearance is varied. In the epithelial types diffuse, alveolar, trabecular and cylindromatous morphology are reproduced. A sarcomatoid pattern is encountered when the cells assume a spindle or fusiform type. The Call-Exner body is distinctive. The hormone elaborated by the tumor cells causes endometrial hyperplasia and hypertrophy of the myometrium. Prolonged vaginal bleeding with or without antecedent amenorrhea is the most prominent complaint and results from endometrial hyperplasia. Vaginal bleeding, enlarged uterus and an ovarian tumor form a triad clinically diagnostic of granulosa cell tumors. Granulosa cell tumors are generally benign and in the early stages are cured by simple removal. Sensitivity of the tumor to irradiation is varied. Cases reported in the literature do not contain sufficient data to warrant a final opinion.

J. THORNWELL WITHERSPOON.

BANTI'S DISEASE AND PREGNANCY; SPLENECTOMY; DELIVERY OF FULL-TERM LIVING CHILD SIX AND ONE-HALF MONTHS LATER

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BANTI'S disease seems to be a very rare coincidence in pregnancy, and very few cases of pregnancy occurring in a patient with this condition have been reported.

Allen¹ reported two cases in 1924. One patient had a splenectomy five years prior to the pregnancy. The pregnancy was normal, except for gastrointestinal disturbances. Labor was terminated by low forceps; the patient suddenly died as the vagina was being inspected immediately after delivery. The second patient delivered a premature child; the delivery was followed by postpartum hemorrhage. Six months later when the patient was six weeks pregnant, a therapeutic abortion and sterilization were advised and done; one month later splenectomy was done and the spleen was found to weigh 885 gm.

Birdsong, Hubert, and Whelchel³ reported a case in 1925 of severe anemia in pregnancy requiring transfusions after delivery. Diagnosis of splenic anemia was made on the enlarged spleen and liver with the profound anemia. The patient improved slowly.

Hamlin⁵ reported a case in 1932 of anemia of pregnancy with an enlarged spleen but does not make a definite diagnosis of Banti's disease.

In 1933 Frùhinhsholz and Michon⁴ gave a very full report of a case of anemia with enlarged spleen in a primipara of twenty-two years. The spleen reached to the iliac crest, and the liver was four fingers below the costal margin. During the last trimester several alarming epistaxes were only controlled by tight nasal packings, and blood transfusions. The only slight evidences of toxemia were slight albuminuria and blood pressure 135/75 during this trimester. She was delivered of a living infant, weight 2,880 gm., by low forceps. Although the spleen was not removed, the authors, after discussing the differential diagnosis, came to the conclusion that the patient had "Banti's disease in the so-called intermediate phase, succeeding simple splenic anemia and preceding the ascitic period. In this phase, nasal and gastrointestinal hemorrhages and urobilinuria are common manifestations." They also remark on the unusual occurrence of pregnancy in a patient with Banti's disease and state, "We have only found mention of one case, that of J. Olmer, of the coincidence of such an affection with the state of gestation."

In 1934 Ashton² reported a case of a patient developing an enlarged spleen immediately postpartum.

Hesseltine⁶ in 1930 reported a case of Banti's disease in pregnancy. His patient was found to have an enlarged spleen and a moderate anemia when three months pregnant. A splenectomy was done at this time, the spleen weighing 600 gm. The liver was also seen to be enlarged and cirrhotic in appearance. The pathologic diagnosis was Banti's disease. The patient made an uneventful recovery from the operation and carried the pregnancy to seven and one-half months, at which time she delivered spontaneously a living child. On the eleventh postpartum day paracentesis was done on account of increasing ascites, 7,000 c.c. of ascitic fluid being recovered. The patient improved rapidly and six months later was found to be in good condition, the liver being still 13 cm. below the costal margin.

CASE REPORT

T. R. (LCH No. 29748), white female, aged twenty-three years, first seen in this pregnancy at the prenatal clinic on Feb. 15, 1935, complaining of amenorrhea, her last menses having begun Dec. 4, 1935. This was her third pregnancy.

Previous Pregnancies.—1. Normal uneventful pregnancy, spontaneous delivery of full-term living child after seven hours of labor, uneventful puerperium, 1933.

2. Home delivery service (LCH No. 3614). In this pregnancy she reported to the prenatal clinic when five and one-half months pregnant. She made 10 visits to the clinic. On her first visit her blood pressure was found to be slightly elevated, 140/92, but did not rise above normal at any subsequent visit. During the pregnancy she had some headaches and dizziness and a slight edema of the ankles. Urinalysis showed slight trace to 1-plus of albumin on several readings in the last trimester. She was hospitalized for threatened premature labor on Oct. 4, 1933, for four days. At this time her hemoglobin reading was 80 per cent and red blood cells 4,300,000. She improved with bed rest and carried the pregnancy to term, delivering spontaneously after ten hours' labor a living male infant weighing 4,480 gm., blood loss 100 c.c. (est.). Immediately after delivery she drew the attention of the attendant to the mass in her abdomen, but although a mass was palpated in the left upper quadrant, its nature was not suspected. She did not return for the usual postpartum visit to the clinic in six weeks.

Third pregnancy: As stated above, she reported to the prenatal clinic on Feb. 15, 1935. At this time physical examination showed the uterus to be enlarged to about the size of a two months' pregnancy and revealed a large mass in the left upper quadrant of the abdomen. She was referred to the medical clinic and admitted to the hospital three days later.

The following history was obtained at this time: After delivery in January, 1934, she felt a mass or "knot" in her left side (as noted above). She was seen by her private physician two weeks postpartum in the treatment of acute tonsillitis. His attention was drawn to the "knot" but he dismissed it as the "ague cake" of malaria. During the next year the mass increased in size, felt heavy, and occasionally caused a dull ache, especially after exertion. She had "nervous spells" in which she had a feeling of impending calamity. She had increasing dyspnea on exertion. Her appetite was good but she noticed that cabbage, cucumbers, onions, and beans caused "indigestion" not noted previously. She was no more constipated than usual. She had no epistaxis, hematemesis, nor melena. Her friends had noticed a yellowish tinge to her skin and sclera.

She had always been healthy except for measles and mumps as a child. She had no history suggestive of malaria. One paternal aunt was said to have had an enlarged spleen but this cannot be verified.

On physical examination the patient was noted to have a large "port-wine stain" on her left cheek. The spleen, identified by the notch, was found to extend below the umbilicus. The liver was felt 5 cm. below the costal margin. The uterus was enlarged to about the size of a two and one-half months' pregnancy. Except for some carious teeth and enlarged tonsils, the physical examination was otherwise negative. Jaundice was not noted at this time.

Laboratory work, done during the next ten days, Feb. 18 to 28, 1935, was as follows: Feb. 18, 1935: Hemoglobin, 56 (Sahli); red blood cells, 2,900,000; white blood cells, 5,250; polymorphonuclear leucocytes, 75 per cent; lymphocytes, 21 per cent; and mononuclears, 4 per cent.

Feb. 19, 1935: Blood Wassermann reaction, negative.

Feb. 20, 1935: Specific gravity, serum, 1.0205; oncotic pressure, 17; serum protein, 4.8; van den Bergh, negative; urobilin, 2-plus; and icterus index, 15.

Feb. 20, 1935: Urinalysis: Color, amber; appearance, clear; reaction, alkaline; specific gravity, 1.012; albumin, negative; glucose, negative; and microscopic, negative.

Feb. 21, 1935: Fragility test, began at 0.50 and was complete at 0.36.

Feb. 23, 1935: Platelet count, 190,000; clotting time, three minutes; and bleeding time, five minutes.

The diagnosis was "splenic anemia, early Banti's disease."

After consultations among the medical, surgical, and obstetric staffs, operation was advised "in order to guard against such complications as hemorrhage from the esophagus, gastrointestinal upsets, and ascites." Operation was performed on the morning of Feb. 28, 1935, the patient being at this time about three months pregnant. It was done under spinal anesthesia (100 mg. novocaine and 10 mg. nupercaine). The abdomen was opened through a high, upper left rectus; paramedian incision swung sharply to the left just below the level of the umbilicus. This gave ample room to remove the spleen. The liver appeared normal except for a 2 by 2 mm. area of scarring at the border. A biopsy was taken including this scarred area. The gallbladder was blue and thin-walled, but three stones each about 4 mm. in diameter were felt in it. The foramen of Winslow was found partially closed by old adhesions. The pancreas was not remarkable. The stomach, pylorus, and duodenum appeared as usual, and the tips of the fingers palpated a normal pyloric ring. The appendiceal region and the lower abdomen were not disturbed because of the pregnancy. The spleen was comparable in size to a normal liver. As first seen it was half again as large as the measurements of the excised specimen will indicate. There were many fibrous adhesions laterally and posteriorly, attaching the organ to the stomach, diaphragm, colon, and tail of the pancreas. These were freed, for the most part under direct vision, with long scissors, after which it was possible to deliver the enormous notched, rubbery viscus from the abdominal cavity. The capsule was slightly thickened, and there was one deeply scarred area on the posterior surface which was hyalinized and measured about 1 by 1 cm. There were one or two other very small areas of scarring. The stomach and pancreas were carefully separated from the large veins and smaller arteries of the pedicle, and the arteries were ligated individually with No. 1 chromic catgut. The spleen was then compressed in order to return as much blood as possible into the general circulation, after which the large veins were ligated. The field was left dry. The pancreas and stomach were not injured. There were no accessory spleens.

Pathologic Report.—Specimen consisted of a very large, fibrotic, congested, fairly firm spleen, weighing 1,100 gm. (normal 150-200 gm.), with a nodular white thickening in one place in the capsule; and a small piece of slightly jaundiced, fairly firm liver with slightly rounded edge. Spleen showed in one section, marked hyaline thickening of the capsule, blood filled and dilated sinuses, small lymphoid follicles; in another section (from the central part of the spleen) larger lymphoid follicles, a few of which had central areas of loosely arranged epithelioid cells giving a granulomatous appearance (Gamma-Gandy nodules). Some of the vessels showed thickening. There was an increase of stroma throughout the pulp.

Liver showed some indistinctness of lobular appearance and loss of columnar arrangement of parenchyma cells, which kept, nevertheless, their normal position with respect to sinuses and bile canaliculi. Cell outlines were clear but their cytoplasm was pale staining and reticular. The Kupffer cells were several times their normal size but did not contain visible foreign material. There was very little blood in the sinuses. Around the central veins there was intracellular brown pigment, probably lipochrome.

Diagnosis.—Banti's disease; fatty degenerative infiltration of the liver.

The patient was given a blood transfusion immediately after operation. She made an uneventful recovery and left the hospital on the nineteenth postoperative day.

Subsequent Course.—She attended the prenatal clinic regularly throughout the remainder of the pregnancy. She had no toxic symptoms. Blood pressure readings

ranged 100/60 to 120/72. Urinalysis was negative for albumin throughout pregnancy. Her appetite was excellent, and she was now able to eat cabbage, cucumbers, onions, and beans without subsequent discomfort. Her only unusual symptom was moderate epistaxis occurring about once a week.

On Sept. 20, 1935 (due date by menses Sept. 11, 1935), she delivered spontaneously after thirteen hours' labor a living, normal female child, weighing 4,385 gm., with 75 c.c. hemorrhage (estimated).

On the fifth postpartum day hemoglobin was 85 per cent; red blood cells were 4,500,000. Examination on the eighth postpartum day revealed uterus and adnexa normal, a large keloid scar in the left upper quadrant of the abdomen, some flattening of the left lower chest with the left breast hanging about 2 cm. lower than the right, liver margin felt 5 cm. below the right costal margin. Puerperium was entirely normal except for one mild epistaxis. She and the baby were discharged in good condition on the ninth postpartum day.

On Nov. 18, 1935, she returned to the postpartum clinic. At this time she felt well and no changes were noted from the above examination on the eighth postpartum day. The baby was examined at the same time in the Pediatric Clinic, and found to be a healthy normal child, having gained 1,500 gm.

She was seen again on Dec. 16, 1935, when four months postpartum and over nine months after the operation. She has had no more epistaxes. Her health has been excellent except for a slight cold for the past three days.

Laboratory work done at this time showed the following: Hemoglobin, 91 per cent (Sahli); red blood cells, 4,830,000; white blood cells, 12,850 (leucocytosis may be due to upper respiratory tract infection); polymorphonuclear leucocytes, 56; lymphocytes, 39; eosinophiles, 2; mononuclears, 2; and basophiles, 1. Clotting time, three minutes; and bleeding time, forty-five seconds.

COMMENT

Pregnancy in a woman with Banti's disease (splenic anemia) would appear to aggravate the disease. As the uterus increases in size in an abdomen already burdened with a large spleen, abdominal discomfort and gastrointestinal symptoms occur. Hemorrhage, alarming epistaxis in one case, may occur during pregnancy and postpartum hemorrhage may be excessive. The characteristic anemia of Banti's disease may be so increased by the secondary anemia of pregnancy that hematopoietic therapy and/or transfusions may be required.

Although pregnancy seems to aggravate Banti's disease, it does not appear that the disease has much effect on pregnancy. In both early and late toxemias of pregnancy, the liver is known to be damaged; in our case the liver was seen, grossly and microscopically, to be degenerated, but the patient did not develop any evidences of a mild toxemia in late pregnancy. Other cases were similar. It seems remarkable that these women, beginning the period of gestation with known liver degeneration, showed such slight evidences of any toxemia throughout the course of the pregnancy.

Treatment of Banti's disease, at least palliative if not curative, is splenectomy; the happy outcome of ours and of the previously reported operative case would seem to indicate that as in other diseases incidental to pregnancy, the treatment is to "treat the disease, not the pregnancy."

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BICORNATE UTERUS WITH OVARIAN, OMENTAL AND PELVIC ENDOMETRIOSIS*

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THE report of this case concerns a white married woman, aged twenty-nine years, born in this country and occupied as a hosiery worker. Date of examination May 6, 1935. *Chief complaint:* Pain in lower abdomen during and after periods. *Family history:* Father living. Mother died of tuberculosis. Two sisters living. Two brothers and one sister died in infancy. Five sisters died of tuberculosis. *Personal history:* *Past illnesses:* Measles and diphtheria as a child. Never previously pregnant. No operation. Menstruation began at age of thirteen years, irregular, moderate amount, lasting from three to five days, always painful during and of recent years pain was worse after periods. Last menstruation April 28, 1935. *Present illness:* Seven years ago she began to have pain in lower abdomen which

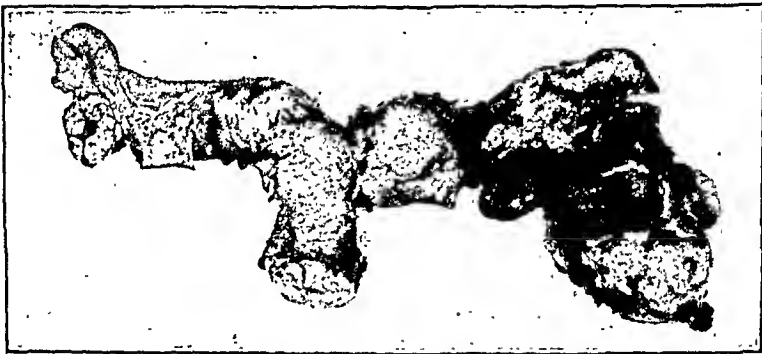


Fig. 1.—Bicornuate uterus with left hematosalpinx and endometrial cyst of left ovary. The left cornu is of the rudimentary type and contains an uterine cavity which is lined by endometrium not communicating with the main uterine cavity, it being separated above by myometrial bifurcation and below to the left a solid stalk of myometrium. The only opening is that which enters the left fallopian tube. The main cornu contains a normal uterine cavity continuous with a single cervical canal and affording a normal avenue of escape for the menstrual flow. The rudimentary cornu must discharge its menstrual contents through the patent left tube. Seemingly supporting Sampson's theory of endometrial propagation by retrograde menstruation and transtubal endometrial implantation.

lasted after her periods. Yellow discharge occasionally between periods. Recently abdominal pain increased in severity. In December, 1934, she was confined to bed with pelvic pain and fever; was treated for tuboovarian inflammatory disease. General physical examination: Negative. Urine and blood work negative except for an increase in blood sedimentation, twenty-five minutes, and slight leucocytosis, 9,000. Abdominal examination revealed tenderness over both tuboovarian regions with a sense of resistance over the left tuboovarian region. Vaginopelvic examination: Vulva negative. Perineum negative. Vagina negative. Cervix posterior, looks and feels normal. Body anterior, lobulated, hard, tender, slightly movable, nodule at left cornu. Right lateral region: prolapsed cystic ovary, tender. Left lateral region: tender, cystic mass independent of uterus. Rectopelvic examination revealed nothing additional.

*Read at a meeting of the Obstetrical Society of Philadelphia, March 5, 1936.

Provisional diagnosis: Uterine myoma, bilateral salpingo-oophoritis, left ovarian cyst. Operation was advised and performed.

Condition found at operation: Omental adhesions wrapped around left ovarian cyst and left cornu of uterus, when freed, exposed cyst and small firm mass feeling

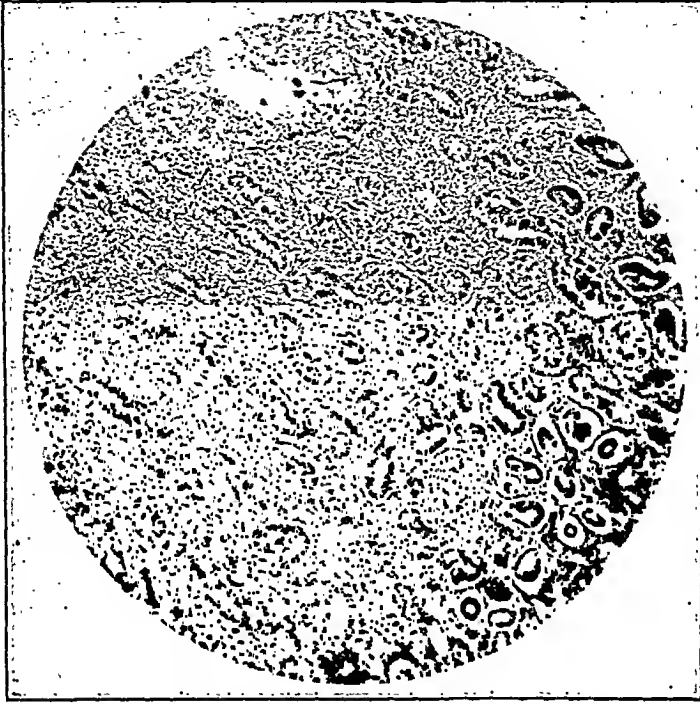


Fig. 2.—Showing endometrium of main cornu in the proliferative stage. Lining of the uterine cavity continuous with a single cervical canal.

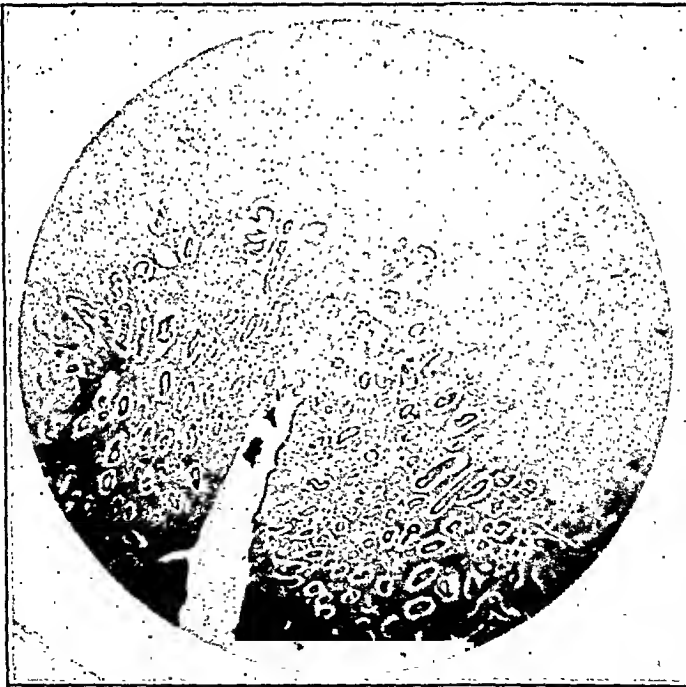


Fig. 3.—Showing endometrium of rudimentary cornu in the proliferative stage.

like uterine fundus. The mass was grown to another mass on the midline which felt like another uterine fundus. Both uterine fundi were united by a distinct myometrial bifurcation. From the left side and at the left cornu, anterior to the origin of

the fallopian tube, the left round ligament emerged. The left tube was enlarged and distended with blood (hematosalpinx) and the fimbria agglutinated to the cyst wall. The additional or rudimentary fundus sprang from the left of the main

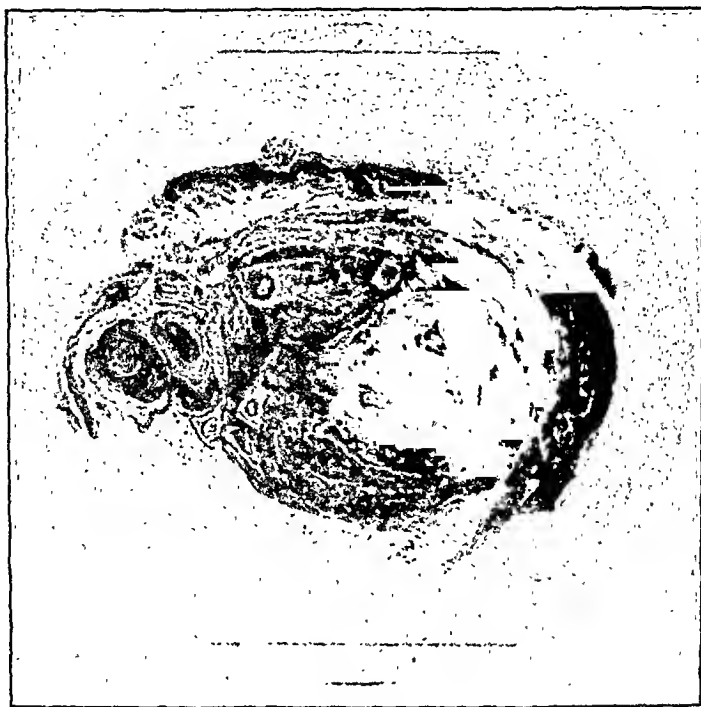


Fig. 4.—A transverse section through solid myometrial stalk by which the rudimentary cornu is attached to the main cornu. Devoid of endometrial elements.



Fig. 5.—Hematosalpinx of left tube, the only escape for menstrual blood from the rudimentary cornu. Showing blood in the tubal lumen and distended mucosal plications.

fundus which was continuous with a single cervix. From the right fundal cornu, the round ligament emerged anterior to the tube which was fused with the right ovary

and adherent to the floor of the pelvis. The left ovarian cyst ruptured while freeing the omentum and exuded a chocolate syrupy material. Bluish black, glistening areas on the omentum and in culdesac.

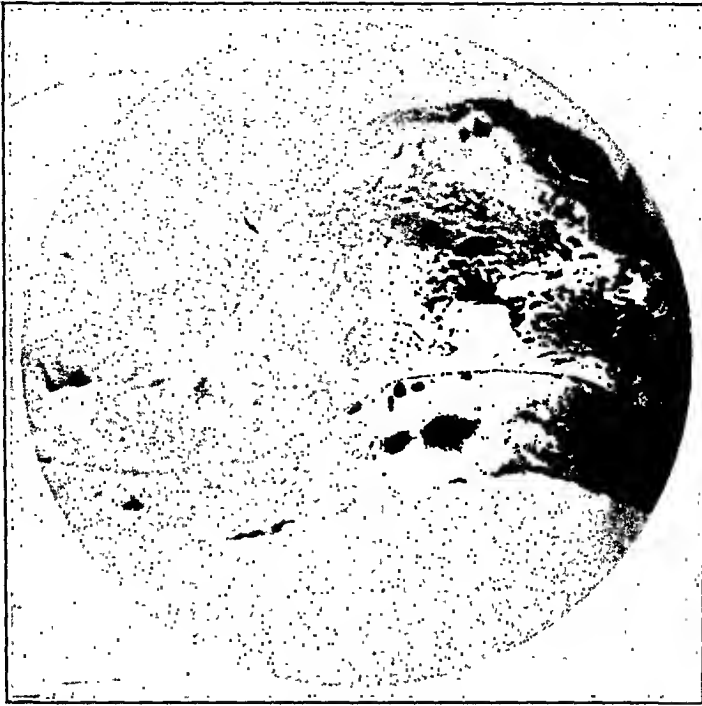


Fig. 6.—Endometrial cyst of left ovary. Showing distended and distorted endometrial glands within the cyst walls.

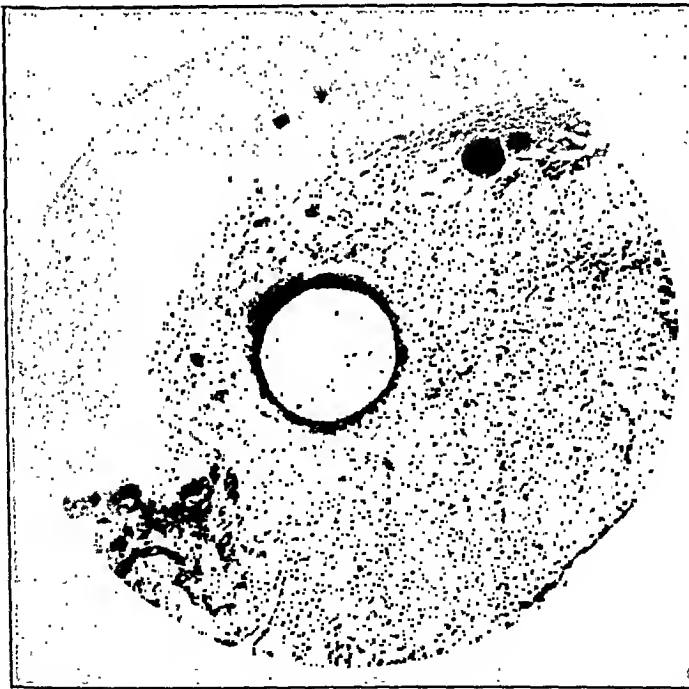


Fig. 7.—Section of omentum showing dilated endometrial gland.

Operative diagnosis: Bicornate uterus with left rudimentary horn, left hematosalpinx, endometrial cyst of left ovary, omental and pelvic endometriosis, chronic right salpingo-oophoritis.

Operation: Total hysterectomy with bilateral salpingo-oophorectomy, resection of omentum.

Final diagnosis: Report of biopsy. Bicornate uterus with uterocornual obstruction on left side. Endometriomas of abdominal cavity. Phagocyte cell reaction of left tube. Abdominal blood clot and omentum.

Comment.—Considering the anatomic pathology, especially stressing the rudimentary left cornu with a uterine cavity lined by normal endometrium and com-

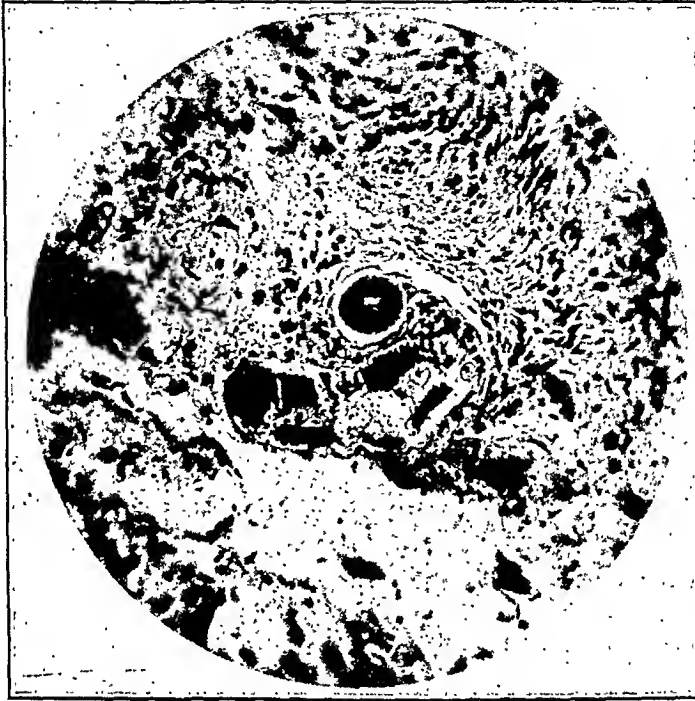


Fig. 8.—Showing several endometrial glands in a group of stroma cells, derived from implants found in the culdesac.

pletely occluded from the main uterine cavity with the exception of an opening at the uterine end of the left tube, the menstrual flow must of necessity have been retrograde and to the left resulting in the endometrial implantations, proliferating, infiltrating and menstruating in response to the ovarian hormones. Sampson's theory.

1504 MEDICAL ARTS BUILDING

Assinder, Eric W.: *Trichomonas and Vaginal Discharge*, Brit. M. J. 1: 882, 1936.

The author stresses the frequency with which trichomonas is associated with leucorrhea, and differentiates the condition from gonorrhea. The two frequently occur together. The author advises the dark-ground condenser microscope as the most effective method of detection of the flagellate protozoa. Clinical signs are soreness, redness of vulva and vagina, with a mucopurulent discharge. Cervicitis and urethritis are present in complicated cases.

In the hands of the author the best results in treatment have been obtained with devegan tablets inserted once or twice daily, used in conjunction with an alkaline or a 1 in 1,000 potassium permanganate douche. Treatment must continue for several months.

F. L. ADAIR AND S. A. PEARL.

BIO-ASSAY OF A GRANULOSA CELL TUMOR

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A SUFFICIENT number of descriptions of the granulosa cell tumor of the ovary have appeared in the literature to acquaint the physician with this type of pathologic lesion. Recent papers have stressed the physiologic activity of these biologically active tumors rather than their pathologic anatomy. Their endocrine function has made pre-operative diagnosis possible in many instances. This type of tumor elaborates a hormone which activates the müllerian tract in a manner similar to that of the estrogenic hormone of the normal graafian follicle.

Almost all our knowledge of the hormone of the granulosa cell tumor is of a qualitative nature. A few semiquantitative evaluations are cited in the literature.

Frank¹ assayed the lipid extract of a granulosa cell tumor and showed its estrogenic activity, but did not report the quantity found in the assay. Schuschania² reported that implants of the white and of the infarcted portions of a granulosa cell tumor were negative for estrogenic hormone. Extracts made from 30 gm. of the compact white cortex were also negative. Extracts of 84 gm. of the bloody infarcted tissue yielded 4 mouse units of estrogenic hormone. This yield, however, is derived more likely from the blood in the tumor than from the tumor substance, since Schuschania's value is only twice the amount found in the blood during the estrin peak in the normally menstruating woman.³ Klasten⁴ and others have demonstrated the presence of this hormone in the blood, urine, and feces in postmenopausal women who had this particular lesion.

I fail to find in the literature any studies which show quantitatively the amount of hormone in the tumor tissue proper. Such studies are necessary to increase our knowledge of granulosa cell tumor physiology. Since these tumors are uncommon and bio-assays are best done on fresh tissue, it follows that this information can be obtained through single specimen reports from scattered sources.

The object of this report is to describe a granulosa cell tumor on which was made a quantitative bio-assay for estrogenic hormone.

Patient referred by Dr. Russel Rypins. The patient was a fifty-eight-year-old white, virgin female. Uneventful menopause, aged fifty-two years. Vaginal bleeding appeared seven or eight weeks before she sought medical attention. The bleeding consisted of spotting for two weeks, after which the flow came to resemble normal menstruation. The bleeding began to subside two days before my examination. *Examination:* Senile vulva with small clitoris. Virginal introitus. Uterus normal size, mobile, with fundus anterior. A 12 cm. mass was palpable in the right iliac fossa. It was firm, nontender, globular, and fixed. A mass 3 by 4 cm. in diameter was palpable in the left adnexal region. It was firm, slightly irregular, and

appeared to be fixed. The vagina and cervix were normal except for the scanty, dark, bloody discharge which exuded through the external os. *Diagnosis:* ? carcinoma of ovaries; ? granulosa cell tumor.

Operation.—(July 11, 1935.) Bilateral salpingo-oophorectomy and supravaginal hysterectomy. The right ovary was found to be senile. The large mass on the right turned out to be an ectopic kidney located in the right iliac fossa.

Pathologic Examination.—(Dr. Margaret Schulze.) *Gross description:* The specimen consisted of the uterus which had been removed supracervically and both tubes and ovaries. The uterus measured 5 cm. in length and 3 cm. in thickness. It showed about 10 small fibromyomatous nodules in subperitoneal and interstitial locations. The endometrial cavity was somewhat enlarged. The general endometrial lining was smooth and showed some pinpoint congestion. There were 3 small mucous polyps, about 0.5 cm. in diameter and 1 cm. in length, arising near the fundus of the uterus. Arising from the left side of the uterine cavity, about 2.5 cm. above the internal os, was a large irregular polyp measuring 7 cm. in length and 3.5 cm. in its greatest diameter. This polyp had greatly dilated the internal os and protruded through it. On section it showed numerous small cystic cavities and a rather edematous stroma. Superficially it was markedly congested.

The tubes measured approximately 10 cm. in length and 0.5 cm. in diameter. No adhesions were present and the fimbriated extremity of each tube was open.

The right ovary measured 3 cm. by 1.5 cm. by 1 cm. It showed one superficial cyst. On section it was densely fibrous and showed no evidence of ovarian activity.

The opposite ovary was moderately enlarged, measuring 5 cm. by 4 cm. by 3 cm. Its external surface was smooth. On cut section it showed a rather fibrous consistency in general, with some areas showing a deep orange yellow pigmentation. These areas appeared to be more cellular than the remainder of the tissue. There were several small superficial cysts not more than 2 or 3 mm. in diameter.

Microscopic description: On microscopic examination the uterus showed a normal senile type of musculature with several small fibromyomatous nodules, showing the typical arrangement of fibrous and muscular tissue. The endometrium was unusually active in appearance for a postmenopausal patient. It was about twice normal thickness and showed many large irregularly shaped glands, especially in its basal portion. Their epithelium was active in appearance and contained glands with secretion. The stroma cells also more nearly approached the type found in younger patients and showed a slight amount of edema between them. A section through one of the mucous polyps showed the usual picture of irregular glands dispersed through an endometrial stroma. The large polyp showed a fibromuscular stroma in which were scattered large islands of endometrium. These endometrial islands showed an irregular glandular picture with dilatation of the glands up to 2 or 3 mm. in diameter.

The tubes showed the usual senile changes. The right ovary was small and sclerotic and showed no evidence of activity. There were a few small corpora albicantia and 2 small retention cysts with a low atrophic epithelium.

The opposite ovary showed a different picture. The stroma, which resembled normal tissue, showed areas where the sarcomatoid tumor cells merged imperceptibly with the stroma. In other areas the more epithelioid tumor cells were quite demarcated from the stroma. Here they occurred in a cylindromatoid pattern and resembled the normal granulosa cells. The picture is that of a sarcomatoid type of granulosa cell tumor with some areas suggestive of the cylindromatoid type. Nowhere was the typical folliculoid picture seen. No mitoses were found. There was no suggestion of malignancy in the histologic appearance.

Diagnosis: Granulosa cell tumor of left ovary (sarcomatoid), fibromyomatous uterus, senile right ovary and tubes, hyperplasia of the endometrium with mucous polyps and an adenomyomatous polyp.

Bio-Assay for Estrogenic Hormone.—The tissue was kept frozen for one week until the animals were ready for the tests. Accurately weighed pieces of tissue were finely minced and transplanted intraperitoneally into spayed, adult, female, white mice. Estrus was determined through examination of the vaginal spreads, using the criteria of Frank.³ The yield of estrogenic hormone was found to be 3.2 mouse units per gram of fresh tissue or 36 mouse units per gram of desiccated tissue.

DISCUSSION

These values can only be considered as approximations due to the inherent errors of bio-assays. They only suggest an order of magnitude for stored hormone. The granulosa cell tumor, like the normal follicle, probably has a greater capacity for the production of hormones than for storage. Because of the absence of similar determinations in the literature, these values cannot be compared with those of other granulosa cell tumors. It seems likely that the different tumor types (folliculoid, cylindromatoid, and sarcomatoid) will have hormone contents which will vary with their histologic pictures. Compared with Schuschania's tumor, the tumor reported here contained at least 65 times as much estrogenic hormone as he found in the bloody portion of his specimen.

In the postmenopausal patient with a granulosa cell tumor, one has an ideal laboratory in which to work out the details of granulosa cell tumor physiology. All patients whose history and pelvic examination suggest this type of pathologic lesion should have the following assays made for estrogenic hormone.

1. Preoperative daily analyses of the twenty-four-hour output of urine and feces to determine the daily production of estrogenic hormone (assuming that an equilibrium exists).

2. Quantitative assay of the fresh tumor tissue by implants, extraction or both.

3. Postoperative daily analyses as in 1, to determine the excretion rate of estrogenic hormone.

Summary: A bio-assay of a granulosa cell tumor (sarcomatoid type) yielded 3.2 mouse units of estrogenic hormone per gram of fresh tissue or 36 mouse units per gram of desiccated tissue.

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- (1) Frank, R. T.: Am. J. Dis. Child. 43: 942, 1932. (2) Schuschania, P.: Zentralbl. f. Gynäk. 54: 1924, 1930. (3) Frank, R. T.: Female Sex Hormone, Springfield, Ill., 1929, C. C. Thomas Co. (4) Klasten, E.: Arch. f. Gynäk. 150: 643, 1932.

490 POST STREET

Lin and Tsou: The Escape of Lipiodol Into the Utero-Ovarian Venous System in Hysterosalpingography, Chinese M. J. 49: 1241, 1935.

The authors report that pulmonary complications from lipiodol embolisms are not rare. The symptoms range from feeling of tightness in the chest to severe cough and even hemoptysis. The discomfort in the chest and cough were evidently manifestations of oil embolism. Hemoptysis in two of the cases reported was most probably the result of small hemorrhagic infarcts in the lungs. Dissolution of continuity of endometrium they believe offers the most plausible explanation.

C. O. MALAND.

A NEW, RAPID, ECONOMICAL TEST FOR PREGNANCY AND CERTAIN GYNECOLOGIC CONDITIONS

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(From the Obstetrical Department of the Miami Valley Hospital)

A GENERAL discussion concerning the action of certain endocrine derivatives brought out speculation as to the appearance of an anterior pituitary-like substance in the urine of pregnant women.

The idea was suggested that if a pregnant woman contained this substance in her system, she might not be sensitive to its intradermal application, and, on the other hand, a nonpregnant woman might show a reaction to its presence. Upon this basic supposition, a series of women known to be pregnant were injected and also an equal number of women known not to be pregnant were likewise studied.

The test consists of an intradermal injection of two minims of fresh antuitrin-S which has been kept in an ice box. We select the ventral surface of either forearm as the site of the injection. An ordinary 2 c.c. hypodermic syringe and 26 gauge needle is used for the intradermal injections. It is important that the skin, syringe, and needle be cleansed with sterile water and not alcohol, as alcohol reduces the potency of the antuitrin. It is also important that a true intradermal injection be made, as deeper injections are not satisfactory.

After introducing two minims intradermally, we wait one-half hour before reading the reaction. If there is a slight reaction, we wait another one-half hour before drawing our conclusions. If there is no reaction at the end of this time, we do not observe the patient longer. Patients thirty years or older delayed the reaction for a longer period, and those near the menopause reacted as late as three hours. If there is a reaction, we usually observe the reaction at the end of two hours, but this is not necessary. The reaction consists of an area of erythema around the site of injection measuring in diameter from 7 to 35 or 40 mm. Occasionally a reaction will reach 5 cm., but usually the area of erythema will measure 25 to 30 mm. If the bleb which is raised by the injection into the skin becomes red, but the skin adjacent and surrounding the bleb does not become red, then this is not a positive reaction. The reddened area overlying the bleb will measure 7 mm. or less. Obviously a negative test is one in which there is no erythema surrounding the point of injection except, as noted above, that which overlies the bleb and measures 7 mm. or less.

A patient who is pregnant or who has aborted and retains some live decidua cells, does not react to the antuitrin-S. A patient who is not

pregnant or does not have any retained living tissue of the products of conception, promptly reacts to the skin test. The reaction in a non-pregnant woman usually begins immediately following the injection or within one to three minutes. In every case that we have observed, a patient who reacts or who gives a positive skin test and negative pregnancy test has a well-defined erythema at the end of fifteen minutes, except as stated above concerning the age. Occasionally a patient who is pregnant or has retained decidual cells will react to the skin test for ten to twenty minutes, but the reaction will have disappeared at the end of one-half hour. These patients we observe again at the end of one hour and have found that their reaction does not return. In three or four instances we have observed a delayed reaction beginning four to eight hours following the intradermal injection. These patients did not react at the end of thirty minutes or one hour, and proved to be pregnant. It has also been our observation that patients who have aborted prior to admission to the hospital, and who have reacted slightly to the antuitrin-S, have very few live decidual cells on microscopic examination of endometrial scrapings. It is interesting to note in these types of cases where the decidual cells are dead or dying, the Aschheim-Zondek report will be negative, whereas the antuitrin test will be positive. If in a known abortion case we get a slight reaction to antuitrin-S, we can say, the remaining decidual cells are loosely attached. We believe there is a quantitative phase to the reaction.

The following are the case reports excepting those tests done on women entering our wards at term or in labor, all of which were positive for pregnancy, these being used as controls and checks on the solution; some thirty or forty have been done to date.

CASE 1.—Mrs. B. B., thirty-two years old. Menstruation regular. Painful, five days' duration. First menstruation at twelve years. Six weeks preceding her visit to my office she menstruated what she considered normal, excepting pain less than usual. At her next menstrual period, two weeks before, slight menstruation with severe colicky pain referred to the right side. Menstruation lasted three days, free one day, and appeared again with pain. A free period of five days again, and then she continued to stain and showed slight staining upon examination. At the time she consulted me, she was free from pain but complained of pelvic fullness and slight rectal spasm.

Examination revealed slightly enlarged uterus, cervix open. In the right broad ligament a mass the size of a walnut, very tender, and pressure caused a sense of nausea and desire to defecate. Antuitrin-S, 2 mm. skin test was made. One hour later no reaction. Diagnosis: ectopic pregnancy. Operation twelve hours later: unruptured ectopic removed.

CASE 2.—Mrs. H. B. A definite counterpart to Case 1. Antuitrin-S was negative; operation, unruptured ectopic.

CASE 3.—Mrs. L. P. Patient had pessary inserted because of sterility. Menstruation had been very painful but regular. Pessary worn three months and removed. First menstruation normal, no pain. Second menstruation missed. Five days later spotting with pain and feeling of faintness, rectal pressure. Three weeks following the missed menstruation a few small clots expressed with pain.

Examination: Mass in right broad ligament; cervix open; body slightly enlarged. Antuitrin-S three different times. Antuitrin-S negative. Patient was in hospital for observation during these tests. Diagnosis: Ectopic. Operation: Ovarian cyst size of golf ball twisted on pedicle.

By these cases our interest was awakened as to the value of this procedure in the diagnosis of pregnancy and in pelvic conditions, especially those directly influencing the ovary and the endometrium. Therefore the following series was carried out:

1. Fourteen cases of abortion, the earliest of whose pregnancy was five weeks and the latest of five months, with an average of six weeks to two months; the antuitrin-S was positive for pregnancy (negative reaction), and the Aschheim-Zondek was positive in all cases.

2. Sixteen cases of abortion, the earliest of whose pregnancy was four weeks and the latest five months (average two months); the antuitrin-S test was positive for pregnancy (negative reaction) in all cases. Aschheim-Zondek tests were not done in these cases.

3. Two ectopic pregnancies (ruptured), one of six weeks' gestation, one of two months' gestation whom we saw three weeks and two weeks following rupture; the antuitrin-S positive for pregnancy (negative reaction); the Aschheim-Zondek negative.

4. Two cases of ectopic pregnancies (ruptured), one four weeks' gestation and one two months' gestation whom we saw two weeks following rupture; the antuitrin-S positive pregnancy; the Aschheim-Zondek positive for pregnancy.

5. Four cases of abortion, the earliest two months' gestation and the latest five months' gestation; the antuitrin-S test positive for pregnancy (negative reaction); the Aschheim-Zondek negative for pregnancy.

6. Ten cases of pelvic inflammatory disease, negative antuitrin-S and negative Aschheim-Zondek. By negative antuitrin-S, we mean negative for pregnancy with positive reaction.

7. One case of hydatidiform mole, two months' gestation. Both antuitrin-S and Aschheim-Zondek positive for pregnancy. No evidence of chorionepithelioma.

8. One case of teratoma of ovary metastatic to descending colon in girl of eight years; both antuitrin-S and Aschheim-Zondek were positive.

9. One case of lymphoblastoma of brain. The antuitrin-S test was positive (negative reaction), the Aschheim-Zondek was questionable.

10. One term pregnancy with eclampsia, the antuitrin-S was positive. One term pregnancy with placenta previa, the antuitrin-S was positive. One term pregnancy with dead fetus, the antuitrin-S was positive.

11. One abortion, five months' gestation, the patient reacted positive to *B. abortus*, the antuitrin-S test was negative (positive reaction). No Aschheim-Zondek was obtained. Probably due to complete death of cells. All other *B. abortus* cases have shown death of decidual cells.

12. Three cases of abortion, the earliest two months and latest three months, all reacted to the antuitrin-S, and gave a negative pregnancy test. No Aschheim-Zondek tests were obtained in these cases. No living cells in placenta.

13. Twenty-four nulliparous patients, who were known not to be pregnant, run as controls. On these cases all antuitrin-S tests were negative for pregnancy (positive reaction). Careful history of menstrual date in controlled girls provided this material.

14. Six patients, one to eleven days postpartum, who remained positive to the antuitrin-S (negative reaction).

15. Two patients, who aborted three months prior to admission to the hospital, whose endometrial scrapings revealed dead decidual-like cells; the antuitrin-S test was negative for pregnancy (positive reaction).

In conclusion, we believe that the antuitrin-S test for pregnancy as carried out by the above method is a reliable guide in the diagnosis of gynecologic problems. To its advantages are the elements of time, simplicity, and economy. From our data apparently the test should show value in any form of pathology that would interfere with normal ovarian function, such as ovarian cyst, etc. The presence of living decidua will give a pregnancy test which should be valuable in diagnosis of missed incomplete abortions. Valuable time can be saved in suspected ectopic gestation. The reaction of this substance intradermally corresponds with the Aschheim-Zondek test in malignant disease. So far it has proved more delicate than the Aschheim-Zondek test in borderline cases. It has shown that the antuitrin-S like substance is present in a woman's system following delivery and this may be a factor in the prolonged lochial flow, especially in older patients who do not have a sufficient amount.

ACUTE APPENDICITIS COMPLICATING LATE PREGNANCY

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REPORTS of acute appendicitis complicating the last trimester of pregnancy are found but infrequently in the literature. I would thus like to add the case report of a pregnancy in the eighth month complicated by a ruptured gangrenous appendix with thrombosis of the appendical vein.

F. A., a twenty-four-year-old white female, was admitted to the Newark City Hospital on May 16, 1934, complaining of abdominal pain which had begun the morning of the previous day. There had been no previous attacks of a similar nature that she could remember. The onset of the pain was followed by nausea and vomiting in several hours. The pain at first was sharp and severe, and soon became localized in the right lower quadrant. She had had a chill and thought she had had some fever. The pain later became stabbing in character, radiating to the right upper quadrant and accompanied by pain in the right shoulder. She vomited several times the night before admission. The provisional diagnosis on admission was acute suppurative appendicitis or cholecystitis with pregnancy.

Menstruation had been regular until Sept. 26, 1933, when the menses ceased. There had been no vaginal bleeding since that date. Delivery was expected the first few days in July. There had been two previous normal full-term pregnancies with spontaneous deliveries. There was no history of any miscarriages.

Physical examination showed a well-developed and well-nourished young woman, apparently acutely ill, and complaining of abdominal, right lumbar, and right shoulder pain. The eyes and tongue indicated dehydration, and there was dyspnea with slight cyanosis. Further general examination revealed no abnormal findings except in the abdomen, which was found to be symmetrically enlarged by a pregnant uterus, extending midway between the umbilicus and the xiphoid process with the fetus in the L. O. A. position. The fetal heart was strong and regular with a rate of 134 per minute. There was direct and rebound tenderness over the entire abdomen especially in the right lower quadrant. There was some tenderness in the right lumbar region. There was moderate rigidity of the abdominal muscles all over the right side. Temperature was 101.6°, pulse 134 per minute, respirations 40.

Laboratory Data: total white cell count 17,400 cells with 88 per cent polymorpho-

nuclears. A catheterized specimen of urine showed no albumin or sugar. There were numerous granular casts and occasional leucocytes with no clumps.

Preoperative diagnosis of retrocecal gangrenous appendicitis with thrombophlebitis was made. Immediate operation was decided upon, but she was given 1,000 c.c. of saline-glucose (5 per cent) solution intravenously because of dehydration preoperatively.

Operation.—Through a high McBurney incision under gas-oxygen-ether anesthesia, the peritoneal cavity was opened, revealing free purulent fluid with a colon odor which welled out of the wound. Fluid was aspirated. The uterus, which was visible on the medial side of the wound, was protected with a warm sponge. The cecum was located at a higher level than usual above the level of the umbilicus. The appendix was firmly adherent, gangrenous, and perforated, lying retroceally. A large fecalith had escaped from the appendix and was found lying free in the abdomen at the base of the appendix. The appendix was removed after ligating the mesentery and the base. The meso-appendix was ligated as high as possible in the hope of getting above the suspected thrombus in the appendiceal vein. An attempt made to invert the stump was not entirely successful due to the position of the cecum. Two Penrose drains were brought through a separate stab wound, one running well up under the liver, the other lying in the right gutter. The incision was closed in layers, placing several silver drains under the fascia. The patient left the operating room in good condition. Operative time, one hour and fifteen minutes.

Postoperative Care.—Continuous duodenal suction was instituted through which she was alternatively given fluids and the bowel contents drained off. She was given fluid by hyperdermoclysis every six hours for the first two days. After the first twelve hours there was no vomiting. Her general postoperative course was not so stormy as might have been expected, considering the extent of the inflammatory process. Postoperative abdominal distention was quite easily controlled. On the sixth day she showed slight vaginal bleeding without pain. This was the only evidence of possible impending premature labor while in the hospital at this time. The wound drained freely of thick foul colon pus, the drainage gradually diminishing to a scant amount at the time of her discharge. The drains were shortened gradually, and finally removed on the twelfth postoperative day. She was allowed out of bed on the fourteenth day; after being up and about the ward for four days, with no apparent ill effects, she was discharged from the hospital on June 3, with the advice to go home and rest as much as possible.

Two days later, on June 5, she was admitted to the obstetric ward early in the morning, strong uterine contractions having begun about an hour previously. The membranes ruptured at 11 A.M., and she was delivered ten minutes later of a living male child weighing four pounds fourteen ounces. Following the delivery of the placenta, a moderate quantity of foul-smelling purulent material escaped from the vagina. A culture of this material and a direct smear both showed a gram-positive diplococcus. Blood Wassermann taken at the time of delivery was negative. The puerperium was uneventful except for a rise of temperature to 100.4° on the third day. She left the hospital for the second time on the tenth day postpartum. Discharge note on the obstetric record read "Premature delivery, no sepsis, puerperium negative."

She was followed in the surgical out-patient clinic for several months. There was a slight seropurulent discharge from the stab wound. During July she complained of upper right quadrant pain. A gallbladder series and a barium enema failed to show any pathology. There was no herniation of the wound. She was discharged from the clinic on Aug. 15, 1934, approximately three months after operation, symptom-free and with no drainage. Routine check-up after one year showed she was in good health. There had been no recurrence of the pain. The wound was well healed and she was apparently in good condition. The baby was well.

IONIZATION METHOD FOR THE TREATMENT OF ENDOCERVICITIS

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ENDOCERVICITIS, undoubtedly a most common gynecologic condition, is very often erroneously treated. In order to evaluate properly the efficiency of the various methods of treatment, a consideration of the underlying pathology and a definite therapeutic aim are essential. In this the following must be accomplished: first, kill the invading organism; second, destroy the infected glandular tissue; and third, provide adequate drainage for the obstructed and infected Nabothian glands.

In the past few years numerous physiotherapeutic methods have been employed in an attempt to attain these aims, but to date there has been no one method which has satisfied all the criteria of rational treatment.

In general, most methods either undertreat, leaving considerable infected area, or overtreat producing tissue destruction, bleeding, necrosis, scar formation, and subsequent stenosis of the cervix. The method of treating the infected cervix by ionization is the most recently adopted procedure in the Gynecologic Out-Patient Department of Temple University, namely, ionization of metallic copper in the cervix by means of a galvanic current that meets the prescribed criteria of ideal treatment.

Technic.—The technic employed, as devised by Tovey,* is as follows: The ionization apparatus delivers a direct galvanic current which is controlled by a rheostat and measured by a milliamperemeter gaged to 25 milliamperes. The instrument has two poles. The negative one is attached to a specially designed indifferent electrode covered with a wet felt pad. To the positive pole is attached the intracervical copper electrode which is made in five sizes, designed to fit the cervical canal without entering the internal os. The wet felt pad connected to the negative pole is placed under the buttocks of the patient. A bivalve speculum is then introduced, the cervix exposed, and secretion removed. The proper sized copper electrode is inserted to the internal os. If the external os is too small to admit even the smallest electrode, the tip of the electrode is introduced and the negative current is turned on slowly. Five to ten milliamperes used for about five minutes causes softening and relaxation of the tissues about the external os, permitting the further insertion of the instrument. After the electrode has been properly placed, the positive current is turned on, the rheostat is turned slowly until the milliammeter registers from 8 to 20 amperes, depending upon the amount of current desired. The larger the area of the electrode in contact with the cervical canal, the greater the amount of current. After a minute or two, the electrode adheres to the cervical mucosa. Cotton is then packed against the cervix surrounding the electrode to prevent its displacement. At the end of fifteen or twenty minutes, crystals of

*Tovey, D. W.: AM. J. OBST. & GYNEC. 27: 916, 1934.

copper oxychloride may be seen to surround the electrode and external os. The current now is turned off slowly, the electrode withdrawn, and the cervical canal is seen to be covered by a layer of copper crystals. Very often, due to superficial electric coagulation and dehydration of the tissues of the cervix, the electrode becomes adherent to the cervical mucosa. This necessitates the use of the negative current for two or three minutes in order to allow the withdrawal of the electrode without undue trauma to the cervical mucosa.

The patient is instructed to take a cleansing douche every night and to return in two weeks for another treatment. It has been our custom to have the patient to return immediately after her menstrual period whenever possible. Four to six such treatments are usually sufficient in clearing up the average case of endocervicitis with erosion.

Most patients have complained of some degree of cramplike pain in the lower abdomen during and for several hours after the treatment. In a few cases the pain was severe enough to confine them to bed for one day, but no other outward effects were noted. In no case has there been any evidence of bleeding or slough.

RESULTS

In the past eighteen months we have treated a total of 93 patients and have given 389 treatments. Of these, 71 patients were discharged as completely cured. The patient returns once in two months for a follow-up. There were 6 complete failures; these patients had a pelvic inflammatory disease with a palpable mass confusing the picture. Seven patients, after receiving the full course of 6 treatments, were relieved of the profuse discharge, but, clinically, were not cured, a definite erosion with edema of the cervix being present. Two of these patients had also a complicating pelvic inflammatory disease. Nine patients did not return after the second treatment.

Although there was no particular benefit in those cases in which there existed a pelvic inflammatory disease, there was no lighting up of infection as often occurs when the cautery is used in this type of case.

CONCLUSION

Our experience with this method leads us to believe that it approximates, more closely than any other thus far advocated, the ideal treatment for endocervicitis. The deposition of copper as copper oxychloride produces a marked bactericidal effect. The mild coagulating property of the positive current causes a shriveling and obliteration of the infected glands, while the technic of treatment keeps the cervix well dilated, bringing all the mucosa and the openings of the cervical glands in contact with the electrode and, what is more important, permitting adequate drainage.

A MODIFIED INSTRUMENT FOR BIOPSY OF THE ENDOMETRIUM

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THE value of the microscopic appearance of the uterine mucosa in the study of functional derangements of the female genital tract has made biopsy of the endometrium an essential diagnostic procedure. Several types of instruments have been devised for this purpose. Burch and Klinger¹ made use of a punch apparatus. Hoffman² employed a narrow curet. The addition of suction, as suggested by Novak,³ is a distinct improvement over simple curettement, as more tissue is obtained for pathologic examination relatively free of blood. The use of a plain "open-end" cannula, also advocated by some, is objectionable because the force required to scrape off a portion of the uterine mucosa must be directed upward toward the fundus of the uterus. This is contrary to good surgical technic, owing to the possibility of perforating the uterus.

The instrument I have devised, with the technical assistance of Mr. H. Peck, of the American Cystoscope Makers, Inc., is somewhat similar to the suction-curet-cannula recently described by Novak (Fig. 1). It consists of a No. 14 F cannula (5) with a uterine curve, the end of which (a) is round and closed. On the convex side of the instrument, an aperture (b) is cut out, whose edge acts as the curet. The obturator (6) has a special coiled spring tip (j) which permits ease of introduction into the cannula and closes the aperture smoothly and completely, thus preventing any injury to the cervix when used. A pin (k) on the obturator fits into a groove in the cannula at (c), assuring complete closure of the apparatus.

For the performance of the biopsy, the patient is placed in the lithotomy position, cervix exposed with a bivalve speculum, swabbed with 0.5 per cent lysol solution, dried, and painted with 4 per cent Tr. iodine. The cervix is grasped with the tenaculum (1), and the direction and length of the uterine cavity are determined by the uterine sound (2). The cervix is then dilated with the gradual dilators (3) and (4) in order to permit the introduction of the assembled cannula beyond the internal os. This usually gives the patient some discomfort, but if done slowly and with reassurance to the patient, the succeeding steps may be performed more rapidly. The obturator (6) is removed, the Y-valve (7) installed on the end of the cannula, and the suction attachment (8) connected at (h). An assistant holds the 20 c.c. syringe and applies suction when directed.

The valve (f) is now turned toward (d), the cannula gently directed to the fundus of the uterus, and then withdrawn as far as the internal os with an upward lift, in order to exert firm pressure of the aperture (b) against the posterior uterine wall. During this maneuver, the assistant applies suction. When the syringe has been drawn out to its full capacity, the valve (f) is turned toward (e), the air expelled, the valve readjusted toward (d) and suction continued. Specimens from two or three different parts of the endometrium are taken. The instrument is then withdrawn completely while suction is maintained. The cannula, the valve, and rubber tubing are flushed out with water and their contents collected on gauze.

Continuous suction as advocated by Novak, instead of hand suction, may be used, but a bottle must be interposed in the system in order to collect the specimen.

The tissue is immediately immersed in 10 per cent formalin and sent to the laboratory for pathologic examination.

The amount of tissue obtained varies with the type of endometrium encountered. The specimen contains practically no blood and is not distorted by the suction.

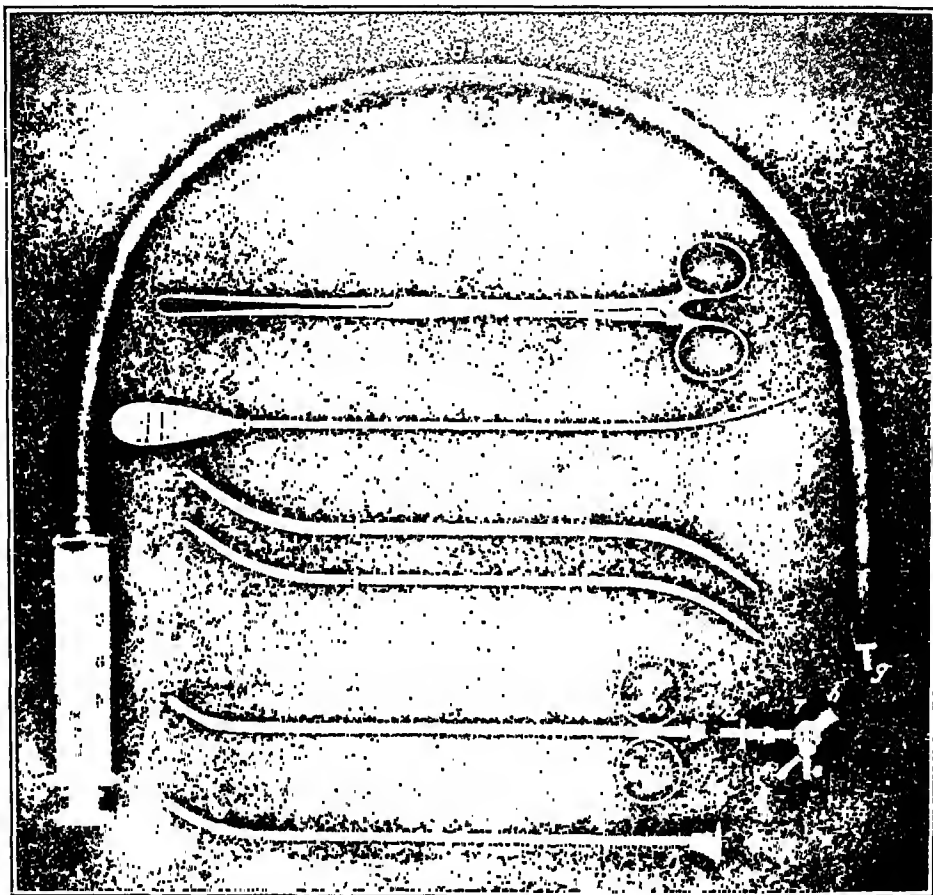


Fig. 1.

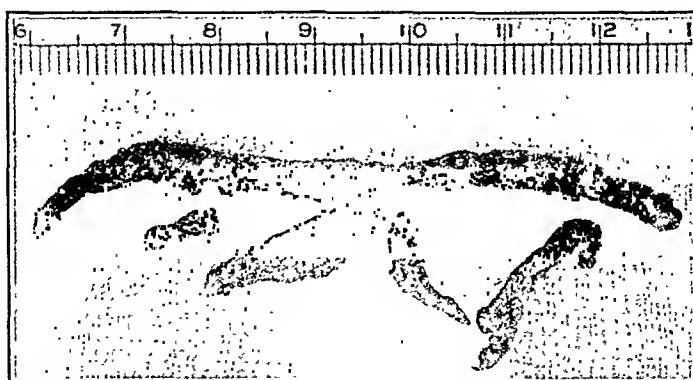


Fig. 2.—Endometrial biopsy in a case of menorrhagia taken on eighteenth day of menstrual cycle.

Fig. 2 gives an idea of the amount of material obtained by this method in a case of hyperplastic endometrium.

This method is not advocated to replace the curet. The diagnosis of suspected fundal carcinoma, uterine polyps and submucous fibroids can only be ascertained or excluded properly by a thorough curettement under anesthesia. Biopsy of the

endometrium is most useful in the study of functional amenorrhea and menorrhagia. Reasonable care should be exercised to exclude a pregnancy or an acute inflammatory lesion before resorting to the biopsy.

With proper precautions to secure sterility, the method may be adopted as an office procedure. Other than a slight bloody show for a few days after the biopsy, no complications have been encountered. With due consideration for its limitations, biopsy of the endometrium, as described above, has proved to be an efficient diagnostic procedure.

REFERENCES

(1) *Burch, J. C., and Klinger, H. H.*: J. A. M. A. 99: 559, 1932. (2) *Hoffman, P. E.*: AM. J. OBST. & GYN. 27: 616, 1934. (3) *Novak, E.*: J. A. M. A. 104: 1497, 1935.

1882 GRAND CONCOURSE

DERMOID CYST DIAGNOSED BY X-RAY

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THE following case is unusual because the diagnosis was established before operation by the roentgen examination, which disclosed the presence of teeth in the patient's pelvis.

Miss C., single, aged twenty-four, consulted Dr. Harold A. Murphy of Jamaica Plain, complaining of pain in the right lower quadrant. The family history was unimportant. She had been well since childhood and worked steadily as a dental hygienist. Her only symptom was dull intermittent pain in the right lower quadrant, of three months' duration. The pain did not radiate, was not accompanied by nausea or vomiting, and was not related to the catamenia, which was regular and normal. An x-ray investigation of the gastrointestinal and renal tracts showed the following:

"The examination of the upper gastrointestinal tract showed that the outlines of the stomach and duodenum were normal, with no evidence of ulcer or new-growth.

"At the six-hour examination the stomach was almost empty and the head of the barium column had reached the hepatic flexure.

"At the twenty-four-hour examination the barium had reached the rectum. There was no evidence of large intestinal dilatation or obstruction. The appendix was not visualized, but the cecum was freely movable and not tender at the time of the examination.

"A study of the gallbladder region showed no evidence of gallstones, and an excellent filling of the gallbladder was obtained with the dye.

"Films of the renal tract showed no evidence of stone formation in either kidney, ureter, or urinary bladder. On the left side of the pelvis, there are several dense shadows, which have the appearance of teeth. One of these shadows seems like a fully developed cuspid tooth with a definite root canal. These are probably teeth elements in a dermoid cyst.

"Conclusions: The examination of the renal and gastrointestinal tracts showed several dense shadows on the left side of the pelvis, which appear like teeth. One of these seems to be a fully developed cuspid tooth. This points toward the presence of a dermoid cyst with tooth elements in it. Elsewhere the gastrointestinal tract is clear, with no evidence of any other pathology."

The patient was then referred to me for a gynecologic examination. The abdomen was relaxed, with no spasm or tenderness. The introitus was virginal, with

no signs of inflammation. On rectal examination a small uterus was found in good anterior position. There were no masses or tenderness in the right side of the pelvis. On the left a tender cystic mass was felt the size of a baseball. This confirmed the x-ray diagnosis of dermoid cyst of the left ovary.

At operation Oct. 16, 1935, at the Faulkner Hospital, the uterus and right adnexa were found to be normal. The left tube was intimately adherent to a cyst of the left ovary and was resected with it. An adherent retrocecal appendix was also removed. The patient made an uneventful recovery and was discharged on the twelfth day.



Fig. 1.

Pathologic Report.—"Gross description: *Cyst*: 8 cm. in diameter, received open. The surface is glistening. The wall measures 2 to 3 mm. in thickness. The lumen is filled with hair and greasy material. The lining in part is skin and in part is smooth and glistening. Bone and fat tissue are present in one place. One tooth is present in a pedunculated mass in the lumen. The tooth is 1 by 0.5 cm. and negative. *Appendix*: 5 by 0.6 cm. The serosa is slightly thickened and pinkish white. The lumen is obliterated. *Fallopian tube*: Negative.

"Microscopic examination: *Cyst*: The wall is composed largely of ovarian tissue. The lining surface is partly formed by squamous epithelium, and in many areas by connective tissue. Hair shafts extend into the cyst wall in places. One projection into the lumen is covered with columnar epithelium and is composed of fat and thyroid tissue. Scattered coil glands are also present. *Appendix*: The lumen is obliterated by fibrous tissue. Muscularis and serosa are negative. *Fallopian tube*: The villi are of average size and negative. The muscularis and serosa are negative.

"Diagnosis: Dermoid cyst, benign. Healed appendicitis with obliteration. Negative fallopian tube."

TRACHEOESOPHAGEAL FISTULA AND COMPLETE ESOPHAGEAL STENOSIS OF THE NEWBORN

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THE case of tracheoesophageal fistula herein described presented a diagnostic and surgical problem. The pathologic findings which ultimately cleared the diagnostic situation are described below, with a diagrammatic representation of the pathologic anatomy.

Mrs. C. P., aged twenty-eight, housewife, of Italian extraction, para i, was admitted to the Obstetric Service of the Lutheran Hospital of Manhattan on Dec. 14, 1935. She had been cared for in the Out-Patient Department and her pregnancy

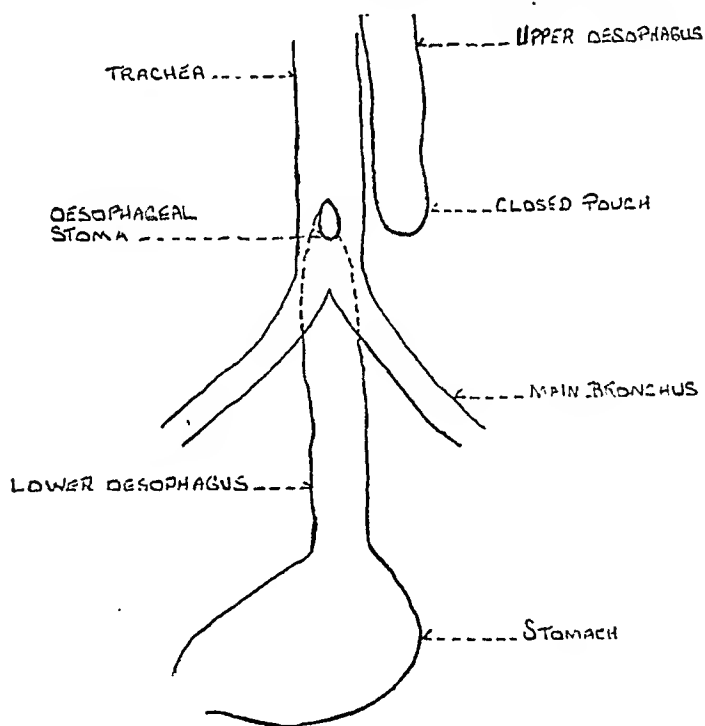


Fig. 1.

had been entirely uneventful. After twenty-four hours of false pains, she fell into active labor and after six hours delivered spontaneously an apparently normal, male child weighing 6 pounds 14 ounces. The infant was resuscitated readily. The perineum was intact, and the blood loss was moderate.

Four hours following delivery the infant was found to be moderately cyanosed, but following the administration of 30 c.c. of blood intramuscularly and brief periods of inhalations of carbon dioxide and oxygen, the color became normal. Twenty-four hours following delivery the infant again became cyanosed and all feedings were promptly regurgitated. The temperature rose to 102°. Cyanosis was marked, breathing was labored and accompanied by sounds similar to those characteristic of pulmonary edema. There were signs of consolidation over the entire right chest.

Pediatric consultation diagnosed aspiration atelectasis over the right chest. Attempts to pass a soft rubber catheter to the stomach met with failure.

A barium feeding was administered, most of which was returned by regurgitation. The plate was taken and the roentgenologist returned a report which carried the diagnosis: "Aspiration pneumonia, entire right lung; congenital stenosis of the esophagus."

The general condition of the infant was poor. Forty-eight hours following delivery cyanosis was intense, temperature 106.6°. Carbon dioxide and oxygen were administered continuously with clyses and stimulants. Feedings were continuously regurgitated. Seventy-two hours after delivery, after consultation, a Witzel gastrostomy was performed as a life-saving measure, under chloroform anesthesia. Post-operative reaction was bad and the infant died six hours after operation.

An autopsy was performed by Dr. Louis B. Ferraro. The esophagus was found divided into two distinct portions, an upper and a lower, with no connection between the two. The upper portion terminated as a blind sac to the left of the trachea and at about the level of the bifurcation. The lower esophagus ran from the cardiac end of the stomach upward behind the trachea to about 1 cm. above the bifurcation where it became narrowed from a diameter of about 1 cm., to a diameter of 3 mm., and opened directly into the trachea. The entire right lung was consolidated.

The accompanying diagram (Fig. 1) illustrates the condition as noted at autopsy. It is apparent that the sole route to the stomach of the infant was by way of the trachea. Feedings probably overflowed or were evacuated from the upper esophagus to be aspirated into the trachea, thence partially distributed to the lungs and partially to the stomach. The gastrostomy was found patent at autopsy, but with the pathology as found, it is highly improbable that it would have proved life-saving even if performed earlier.

This type of case serves to demonstrate an unusual and interesting congenital anomaly rarely seen. More important, it serves to focus attention upon the importance of complete physical and laboratory studies of the abnormal newborn and the value of necropsy where fatalities occur. More intensive study may serve to eliminate the familiar "cerebral hemorrhage," "prematurity," and other diagnoses commonly applied to the problem of the neonatal mortalities.

272 W. 90TH STREET

509 W. 155TH STREET

Shelanski, H. A.: Studies on *Trichomonas Vaginalis* in Vitro, J. Lab. & Clin. Med. 21: 790, 1936.

In studies made on artificially cultured *Trichomonas vaginalis* the following observations were made: With lethal concentrations of picric acid, silver nitrate, silver picrate, protargol, argyrol, and sodium picrate in four dilutions, viz., 1-100, 1-500, 1-1,000, and 1-5,000 in distilled water, the organisms ceased their motion, became distorted, the body membranes ruptured and the contents disappeared in the medium. With lethal concentrations of picric acid and sodium picrate, the organisms assumed a spherical appearance and the membranes burst. Freeing the organism from culture medium and suspension in Ringer's No. 2 solution rendered them more easily susceptible to the action of the substance being tested, thus demonstrating the "buffering" action of the culture medium. Comparisons were made by studying the effect of silver picrate and silver nitrate in vitro. If the separate rôle of the cation is disregarded, it was noted that silver picrate is effective at lower silver concentrations than silver nitrate. Strong silver protein shows a killing power similar to silver picrate; mild silver protein is relatively ineffective, showing its first effect at a concentration of 0.25 mg. of silver per c.c. in eight and one-half minutes.

W. B. SERBIN.

A BABY WEIGHING FIFTEEN POUNDS TWO OUNCES AT BIRTH

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UNUSUAL facts relating to newborn babies have been attracting considerable interest since the birth and development of the Dionne quintuplets in 1934. Twice recently attention has been directed to California by the announcement first, of the birth of an infant weighing over 14 pounds, and second, a little later a living child weighing less than a pound.

In November, 1935, I delivered a woman of a living child weighing over 15 pounds. Such a size stimulated investigation of the recorded births of large children.

The largest child on record, so far as I can learn, was reported by Dr. D. P. Belcher, Sale City, Georgia, in 1916: It weighed 25 pounds. In 1922, Dr. E. Lawton Moss, in the *British Medical Journal*, reports a stillborn female infant weighing 24 pounds and 2 ounces, which specimen is still preserved. Dr. Willis S. Cooke reports through the *Journal of the American Medical Association*, 1916, his delivery of a living male child weighing 18 pounds. In 1927, Dr. F. R. Parakh of Bombay, India, reports a 16-pound baby stillborn after a normal eleven-hour labor.

These are illustrations of different weights but not a complete record of all instances of large infants reported through journal accounts. Most of these infants were stillborn, and one difficulty seems common, in that the delivery of the shoulder always presents a problem.

One naturally turns to the large maternity hospitals and their records of the men of great experience with access to still larger compilations to ascertain their figures. No authority investigated has reported any excessively large infants. These men of authority agree that babies weighing over 11 pounds at birth are unusual, although all have witnessed personally 13 and 14 pound infants.

In view of the above, my experience seems of sufficient value to report. Mrs. J. P., aged thirty-three, of French descent, came to my office first on Aug. 17, 1935. She was a para viii. Three children were living; one died at five and one-half years, the second at eight months, and the third at three weeks. My records do not show the cause of any of the deaths. Her smallest child weighed 9 pounds. In 1929, I delivered her of her fourth baby, which weighed 13 pounds. She was in labor six hours and the delivery was not particularly difficult. The baby's cord was 42 inches in length.

She had had no operations and no illnesses. She is a very large, stout woman. In August, she weighed 300 pounds and since then, as my office scales will only register up to that amount, no further record could be kept.

Her last menstruation began "the last of February, 1935." She felt life first on July 16, 1935. Her blood pressure was 120/70, which rose gradually to 190/110 on November 16, when she showed two-plus albumin, dropping down to 150/90, and no albumin on November 19. She complained of swelling of her face, hands, and ankles beginning November 16, but her physical aspect was such that her word had to be relied upon for that condition. There was no edema present. She was so fat that when she sat in the examining chair, her abdomen extended forward to her knees.

Fetal parts could not be definitely outlined, but a little more resistance on the left seemed to indicate O.L.A. The fetal heart tones were heard on that side.

Measurements made with great difficulty from the symphysis to the upper edge of the fundus were 43 cm. Pelvic measurements were not to be considered accurate.

She went into labor in her home ten miles out in the country a little before midnight on Nov. 22, 1935, and was seen first shortly before 2:00 A.M., when she was having pains every three minutes, very hard.

Examination was made difficult by the fact that the rolls of fat from her abdomen extended to below the vulva and had to be held out of the way continually during the labor. Vaginal examination showed the large vagina full of membranes, the cervical os completely dilated and the baby's head barely engaged. The membranes ruptured during the investigation. Her pains continued about the same.

She began to bear down in about one-half hour and the baby's head was separating the vulva a few minutes later. At this time 0.5 c.c. of pituitrin was given, and her abdomen with contents which had been flopping to her left was held as near the median line as possible in order to assist the uterus in its effort to expel the baby, lest too much force be expended in merely lifting the tremendous mass to midline with each contraction.

Three-fourths of an hour later, after the baby's head had advanced nearly to the point of delivery, the mother was given $\frac{3}{4}$ c.c. of pituitrin again, a dose which is practically never given prior to delivery, but seemed indicated when considering the probable size of the baby and the situation.



Fig. 1.—Author's case compared with a $9\frac{1}{2}$ pound baby.

Shortly after this, the vulva was pushed back over the baby's head, but the shoulders did not come. Very slight traction was made on the head, slight because of fear of hanging the baby, but still the shoulders did not appear. During the pains, the Kristellar maneuver was used, but without result. Pushing up one hand by the baby it encountered the posterior shoulder, the left as it was advancing through the superior strait. By hooking a finger in the posterior part of the baby's axilla, traction was steadily maintained, at first without the slightest progress.

The baby was making attempts to breathe; consequently, once or twice the hand was removed in order to give the baby an opportunity to get some oxygen, although no air seemed to be received. Finally the shoulders made slow progression. A finger finally reached the elbow, and the baby's left hand and arm delivered, then with considerable difficulty, by rotating the posterior shoulder anteriorly, the baby's right shoulder gradually came through under the symphysis. The body and hips followed rapidly. The cord was 36 inches long and had a figure-of-eight knot in the middle. With gentle persuasion, the baby soon began to breathe, although according to the father, who said he was watching the clock, fifteen minutes had elapsed since the baby's head was delivered.

The baby appeared enormous. According to the spring scales on hand, she stretched them to 15.5 pounds. As the baby's cyanosis did not clear readily, the parents were persuaded to grant permission to take the baby to the hospital for the

administration of oxygen. At the hospital, she was again put on scales, weighing 15 pounds and 6 ounces. The circumference of her head was 37.5 cm., breadth of shoulders 21.5 cm., and length 61 cm.

Oxygen was given intermittently, and her cyanosis gradually became better, but had not fully disappeared forty-eight hours later. For several hours immediately after birth she gave short, expiratory grunts, although she cried fairly lustily.

Both arms were completely paralyzed, dangling loosely at her sides; she made no attempt to move them either voluntarily or upon stimulation. Thirty-six hours later, she moved the right arm fairly well and the fingers of the left. At this time she left the hospital.

Examination of her shoulders did not suggest any broken bones. X-ray revealed no fractures, but that her heart was enormously enlarged, principally on the right side. By estimation, it appeared to occupy one-half of the chest cavity. There were no unusual sounds heard anywhere over the cardiac region; still with the x-ray shadow and the persistent general cyanosis, the presence of some congenital heart anomaly is suspected.

The baby was seen again December 21, when she was four weeks old. All cyanosis had disappeared. A fluoroscope was not obtainable. She had attained the full use of each arm. The mother said she was careful with the left for about two weeks, when she ceased to give any particular attention, and since then the baby appeared to have normal use of both arms.

AN IMPROVED UMBILICAL CORD CLAMP

A PRELIMINARY REPORT

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THE consistent use of a cord clamp in preference to an umbilical tie may largely avoid complications such as hemorrhage and stump infections.

Since Willson* in 1922 recommended the use of an umbilical cord clamp, a wide variety of such instruments have appeared. The present clamp was devised in an effort to include the advantages and to remedy some of the faults of previous instruments. It has to date been used in over 200 cases without a single incidence of hemorrhage or infection. The cord stump separated on an average of 5.94 days, leaving a clean, healthy base.

The instrument† herewith presented is made of stainless steel and is extremely durable. Assembled it weighs slightly over one-half ounce. It consists of (Fig. 1) two "half-moon" stainless steel jaws connected by a hardened and tempered carbon steel spring, cadmium plated. These opposing jaws are faced with transverse, sharp, machine-cut teeth which point toward the rear of the clamp. This feature prevents the cord from slipping toward the mouth of the instrument during its application. A rectangular trough on each jaw prevents lateral sliding of the cord. On the flat surface of each jaw is a through and through window which facilitates drainage and drying of the instrument following sterilization. The two central holes admit the prongs of the applying forceps. The latter instrument is designed to permit parallel opening of the jaws of the clamp to a maximum without straining or "setting" the steel spring. Slots on the handles of these forceps provide a sure grip for the hand.

*Willson, P.: AM. J. OBST. & GYN. 3: 506, 1922.

†Manufactured by The Gomeo Surgical Manufacturing Corporation, Buffalo.
Received for publication, April 17, 1936.

For use, the applying forceps is fitted to the clamp and its jaws widely opened. The clamp is then carried on to the cord as close to the skin edge as possible. Care should be taken to bring the cord well to the rear of the instrument. The forceps is then removed. A hemostat is then placed on the cord distal to the clamp and the cord cut between them. Ordinary cord dressing is then applied. As the cord dehydrates, the pressure of the steel spring about the thinning stump is automatically and progressively increased. As previously stated, the stump separates on an average of 5.94 days.

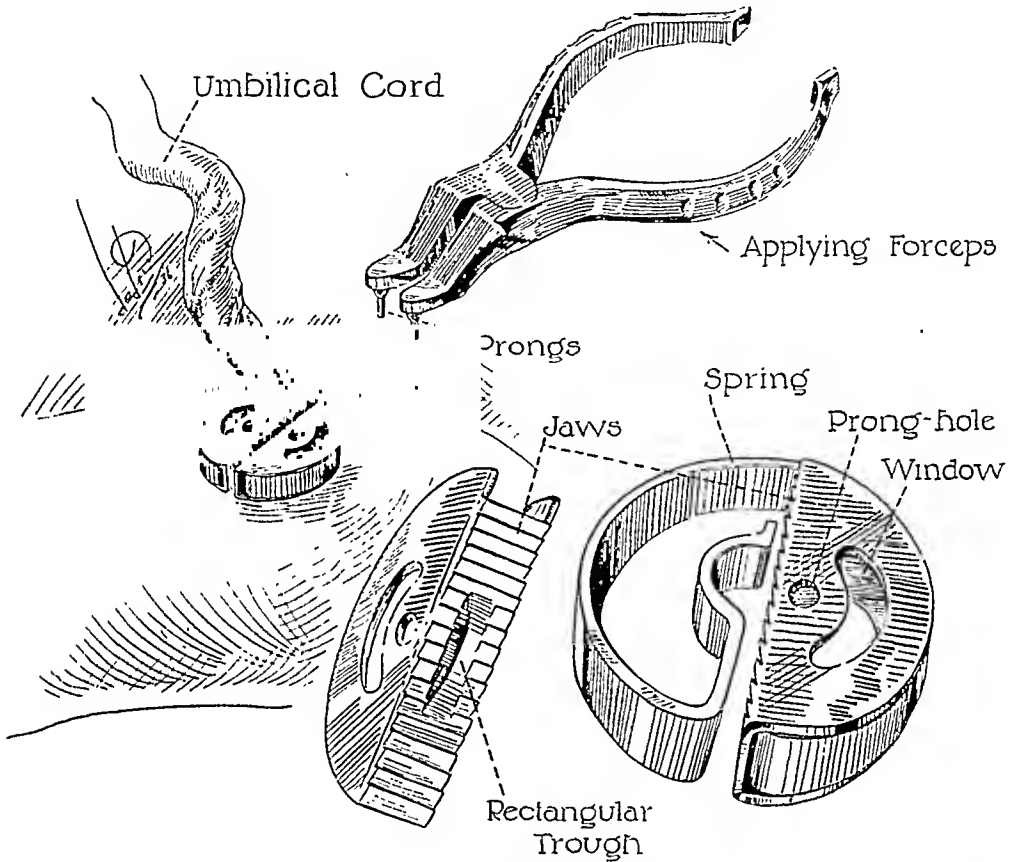


Fig. 1.—Umbilical clamp. Disassembled for detail, applying forceps, and in position on cord.

This improved umbilical clamp seems to provide an ideal method for treatment of the cord of the newborn because of these advantages: (1) It is light in weight and durable. (2) It is thoroughly and completely sterilizable, thereby reducing the likelihood of infection. (3) It is easily and quickly applied. (4) It provides a positive cord grip thereby preventing hemorrhage. (5) On separation, it leaves a clean healed stump.

40 NORTH STREET

The author is grateful to the Obstetrical Staffs of the Buffalo Hospitals for their cooperation and to Cecil Coghlan, M.B., F.R.C.S., F.R.C.P., of Sydney, Australia, for his valued suggestion.

PALPATION OF THE FETAL HEARTBEAT THROUGH THE MATERNAL ABDOMINAL WALL*

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PALPATION of the fetal cardiac impulse through the maternal abdominal wall is quite unknown. Fomenko reports this finding in a case of universal hydrops of the fetus. I was unable to find any other reported in the literature, although some may have escaped my search.

This apparently rare observation was made accidentally, and the following case report is given more as a matter of interest in the unusual than for any practical value it may have.

On April 23, 1933, Mrs. J. S., para iv, was admitted to the Kensington Hospital for Women in labor. According to estimate, based upon the menstrual history, she was seventeen days past term. Her pelvis was ample. Her previous labors had been easy and terminated spontaneously. On admission, she stated that she had had feeble and irregular pains for nine hours. Examination at this time showed the fetus lying longitudinally, with a rounded prominence on the left side. The head was presenting at the pelvic brim. The fetal heart sounds were heard in the left lower quadrant, and the rate was 140. Rectal examination revealed an uneffaced, soft cervix with about 2 cm. dilatation. The presenting part was not engaged. Eight hours later vaginal examination disclosed the cervix as effaced, 8 cm. dilated, and very soft. The presenting part was still above the spines. The brow was found presenting and the position was frontodextra transversa. External examination was rechecked carefully, and at this time the fetal heartbeat was found to be easily palpable through the thin maternal abdominal wall. The rate was 156 while the maternal pulse, simultaneously, was 80. The patient was prepared, and a moderately easy podalic version and extraction were performed. The baby was in good condition, weighed 7 pounds 9½ ounces, and showed the typical caput and molding, though slight, of a brow presentation.

We had here all of the conditions necessary for palpation of the fetal heartbeat through the maternal abdominal wall. The fetus was in a deflexion attitude with its left chest anterior; the membranes were ruptured, and the maternal abdominal wall was thin.

From a theoretical standpoint, in order that this phenomenon may be observed, the fetus must be in an attitude of extreme deflexion with the chest extended and pressing against the uterine wall. Also, it is necessary for the left chest to be anterior.

Since brow presentation is rare, there is not much opportunity to attempt to palpate the fetal cardiac impulse in utero in this presentation. Face presentations, however, are more common and we might some time palpate the fetal heartbeat when other favorable conditions exist, i.e., ruptured membranes and thin uterine and abdominal walls.

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Fomenko, B. P.: Zentralbl. f. Gynäk. 50: 231, 1926.

*Presented at a meeting of the Obstetrical Society of Philadelphia, March 5, 1936.

A PAD FOR KEEPING THE PATIENT DRY IN BED IN CASES OF VESICOVAGINAL FISTULA

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PATIENTS having inoperable, vesicovaginal fistulas suffer much distress from being constantly wet. At night, the necessity of getting out of bed, in order to remove wet clothing, interrupts their sleep to such an extent that a full measure of rest is impossible. Furthermore, the heat of the body hastens the decomposition

Fenestration showing towels beneath

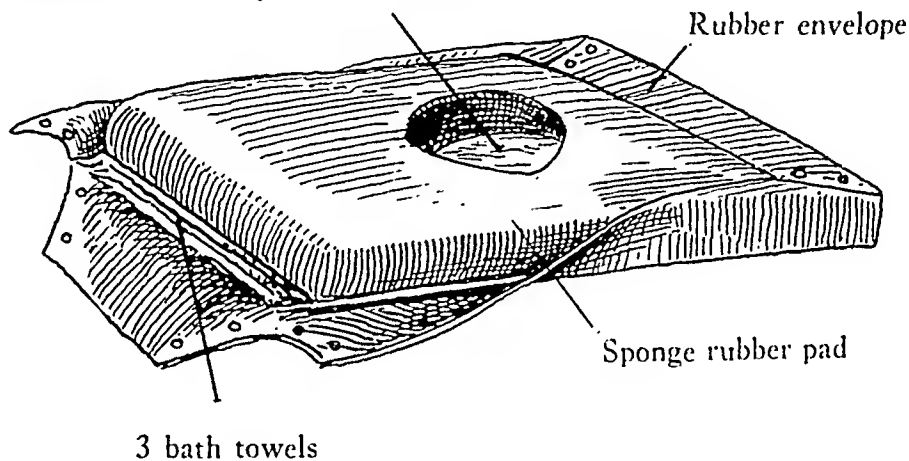


Fig. 1.

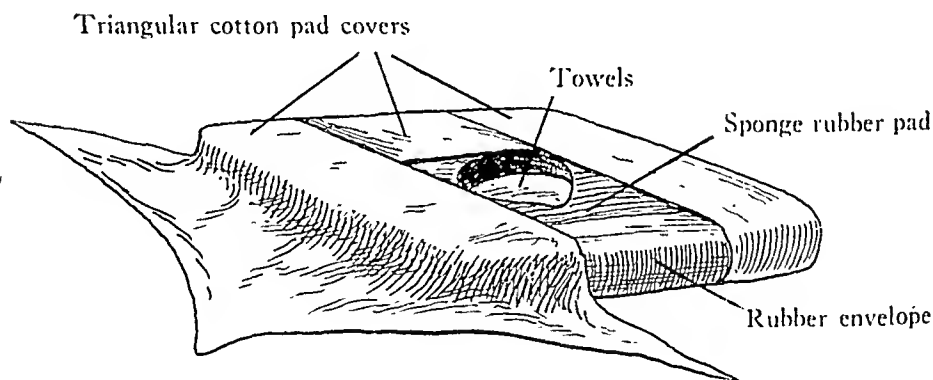


Fig. 2.

of the urine, which is absorbed by the clothing, with the production of the well-known disagreeable odor, distasteful to patient and family alike.

The device shown in Figs. 1 and 2 eliminates the above difficulties, for by its use, the patient is able to remain dry, and at the same time experiences no odor of decomposing urine.

The apparatus consists of two parts, a rubber pad and an envelope. The pad is made of sponge rubber and measures 18 by 24 by 3 inches. It possesses a centrally placed fenestration, measuring approximately 8 by 8 inches, which is somewhat the shape of a toilet seat. The sponge rubber is entirely covered by having cemented to its surface a sheet of smooth, soft texture rubber.

The envelope fits the pad, for which purpose its corners are mitered and supplied with metal snap fasteners; it is made of the same fine quality rubber sheeting as is cemented to the pad. Additional equipment includes bath towels to absorb the urine, and three triangular pieces of cotton cloth, to protect the patient's body from the rubber.

The bed is prepared for sleeping in the usual manner. Several bath towels are placed in the bottom of the rubber envelope, and upon these is laid the rubber pad. The corners of the envelope are then fastened. Next, the pad and envelope are placed across the bed with the tapered end of the fenestration toward the foot. The pad is covered by using the three triangular pieces of cotton cloth as shown in Fig. 2. The two pieces covering the ends of the pad are applied last, since they are the ones which might possibly get wet. Either of these end pieces can be removed independently, without the patient being required to get out of bed to do so. In actual practice, however, the wetting of these covers is very rare.

In order to create an even sleeping surface, patients can make themselves comfortable by utilizing pillows. The consistency of the sponge rubber pad is such that the patient is not conscious of its presence when awake, and she can assume any position during the night and still remain dry.

The patient lies with her vulva overhanging the fenestration in the pad. The urine drops through the fenestration and is absorbed by the toweling, where it spreads out beneath the pad, and thus is not exposed to the patient's body heat. As a result, no offensive odor is produced. The following morning, the moist towels are removed, the pad and envelope are cleansed with a damp cloth, fresh towels replace the moist ones, and the apparatus is again ready for use. The rubber fails to absorb any odor from the urine.

The device was developed through the cooperation of Mrs. S. M., a patient in the Philadelphia Home for Incurables, who has been using it constantly for more than two years. She had suffered from vesicovaginal and rectovaginal fistulas for more than eight years before she had the opportunity of using the present apparatus. She has found the bed pad to be the only satisfactory method for keeping herself dry at night.

Sharman, Albert: The Significance of Leucorrhoea, Brit. M. J. 2: 1199, 1935.

Excessive leucorrheal discharge may arise from vagina, cervix, or uterus. The least common is the latter. Fallopian tubes are rarely the source of vaginal discharge, except in tubal carcinoma, which may cause a watery discharge.

Cervical infection is the most frequent source. Often erosions are seen, or lacerations or ulcerated and hypertrophied areas. Endocervicitis is frequent. Organisms found, excluding gonococci, are diphtheroid bacilli, coliform bacilli, staphylococci, anaerobes and gram-positive diplococci. Syphilitic or tuberculous lesions are uncommon but must be borne in mind.

The vagina is a frequent source of leucorrhea, due to infection and secondary to endocervicitis. *Trichomonas vaginalis* is the most common infective group. The discharge in this type of infection is copious, watery, yellowish, finely frothy or foamy and irritating. The vulva may be inflamed and the vaginal walls may be covered with hyperemic or granular areas.

Treatment depends on the diagnosis of the source of the discharge which must be established. A careful clinical examination is essential. Particular care must be given immediately after menstruation owing to the recurrences at this time.

In noninfective cases local treatment is useless, and general medical measures must be instituted.

F. L. ADAIR AND S. A. PEARL.

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

Announcement

Beginning with the present issue, a comprehensive article on some practical topic or question will be included at frequent intervals, in each volume of the JOURNAL. While addressed primarily to the practitioner, these contributions should prove of general interest. Suggestions as to future topics are invited from our readers. This Department will be conducted by William J. Dieckmann, Associate Professor of Obstetrics and Gynecology, University of Chicago.

THE EDITORS.

THE TREATMENT OF PLACENTA PREVIA

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A VOLUMINOUS literature has accumulated on the treatment of placenta previa. A careful perusal of this literature reveals certain trends in the management of this complication. As in other medical conditions, the pendulum of therapeutic thought swings widely from one extreme to the other, but slowly and surely these excursions grow shorter, so that out of all these experiences a sane, rational and safe therapy has evolved. Few medical conditions are amenable to a specific form of treatment. Usually, the desired end-result can be achieved by a number of methods. It is thus in the treatment of placenta previa.

Although the exact nature of placenta previa was known to such early writers as Portal in 1685 and Justine Sigmundine in 1690, almost no progress was made in the treatment of this condition until comparatively recent years. A maternal mortality of 40 per cent in the expectant treatment (Müller) could be ascribed to an "act of an all-wise providence" in 1877, but an avoidable mortality of even 5 per cent bears the most careful scrutiny today. We, as obstetricians, have become mortality-conscious, partly through our own efforts and partly through the efforts of an ever increasing interest in maternal mortality by the lay public. It therefore behooves us to review the present trends in treatment and to crystallize our opinions on the best management of placenta previa.

The incidence of this complication has changed little by the passing of time, nor is it affected by race or climate. An ever increasing number of patients is referred to hospitals, so that the incidence in hospital practice has been increasing, and is much higher than in the general population. Hauch collected all the cases occurring in Denmark during the five-year period preceding 1933, and found 718 cases in over 346,984 deliveries, an incidence of only 2.07 per thousand, although this

frequency increased to 10 per thousand in hospital practice. In 12,640 deliveries at the new Chicago Lying-In Hospital from 1931 to 1936, the incidence of placenta previa was 9.02 per thousand.

It has been emphasized in the literature that placenta previa is associated chiefly with multiparity, becoming more common with increasing parity. Recent statistical studies tend to indicate that the condition is at present only twice as common in the multipara as in the primipara; 35.1 and 64.9 per cent in the Chicago Lying-In Hospital, 39 and 61 per cent in Marr's report. When one takes into consideration the size of the average American family, the present trend in incidence is equally divided between the primigravida and the multigravida. It is interesting to speculate on this change in trend. The probable explanation is the ever decreasing size of the American family, the decrease resulting in fewer mothers of high parity.

The treatment of placenta previa must be aimed at the following principles: (a) the bleeding must be arrested; (b) the pregnancy must be terminated; (c) infection must be guarded against; (d) trauma must be avoided; and (e) the patient's general condition must be maintained. The method or methods that can accomplish these results with the lowest mortality for the mother and her child should be regarded as the procedures of choice.

PROCEDURES USED

There is no expectant treatment for placenta previa. The opinion is universal that with rare exceptions active treatment should be instituted as soon as the complication makes itself evident. The following procedures have been advocated and used extensively in the active treatment of this condition.

1. *Manual dilatation of the cervix*, or accouchement forcé. This has no place in the treatment of placenta previa. It is probably the most disastrous of all the obstetric procedures for the mother, resulting in extensive lacerations and uncontrollable hemorrhage. The pathologically vascularized cervix tears like wet blotting paper when it is unduly stretched, opening up large, thin-walled sinuses. The resultant hemorrhage may be impossible to control. This procedure has no place in the present therapy of placenta previa.

2. *Vaginal tamponade*, the oldest of the methods, has few advocates today. Packing for the control of hemorrhage had many enthusiastic followers. Before the advent of good hospitals, and good roads for the transport of patients to these hospitals, vaginal tamponade may have been a life-saving measure. The method became obsolete when it was demonstrated that few cases could be packed so satisfactorily as to control the hemorrhage, that the pack as generally used acted as a plug, damming back a continued blood flow. Furthermore, many patients who survived the blood loss succumbed to the infection introduced or activated by the pack. Packing as a preliminary measure before transferring a patient to the hospital is likewise to be condemned because of the danger of infection. It should rarely be necessary to pack a patient before she is sent to a hospital.

Should packing become necessary, the following procedure can be carried out. The pack should consist of ten or twelve yards of three-inch specially prepared gauze which should be moistened just before using. Acriflavine, 1 per cent, in glycerin can be used as an antiseptic. The placenta is separated for a distance of at least 2 cm. about the os. The cervix is fixed by vulsella forceps, and the lower segment, fornices of vagina, and vagina are thoroughly packed. A vulval pad and T-binder are applied. When the course of the patient's labor indicates complete dilatation of the cervix, the pack is removed and delivery completed by podalic version and extraction.

3. *Rupture of the membranes* for the treatment of placenta previa was popularized by Justine Sigmundine in 1690. It has survived the many changes instituted in the treatment of this obstetric complication and has a distinct place in present

therapy. Rupture of the membranes accomplishes a threefold purpose. It allows the rigid placenta to remain attached to the progressively developing lower uterine segment, thereby avoiding any further separation of the placenta which accounts for the hemorrhage. The draining away of the liquor amnii allows the fetal presenting part to descend into the pelvis and to exert pressure against the placenta and the maternal sinuses, thereby controlling further bleeding. Last, it usually initiates labor. In marginal placenta previa this simple procedure is usually sufficient to control the hemorrhage. In partial placenta previa it may not suffice to control the bleeding and in such an event it represents a preliminary maneuver to be followed by another procedure which will more effectively control the bleeding. Essen-Möller reported that in 96 of 245 cases of placenta previa treated by this method, only one death occurred; Olow of Stockholm reported a mortality of 2 per cent; no deaths occurred in the Chicago Lying-In Hospital series.

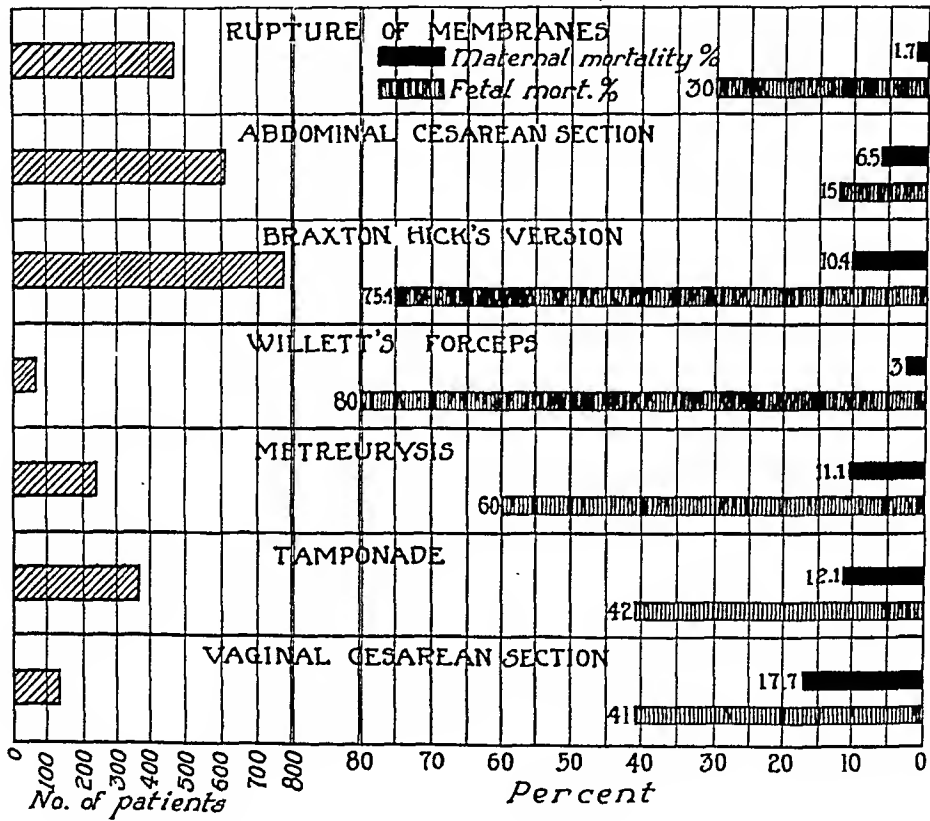


Chart 1.—Analysis of 2,631 cases of placenta previa from representative clinics.

From the foregoing and other statistics, it can be seen that in selected cases where this method is applicable and controls further bleeding, the results for the mother are good. The simple procedure can be carried out with little manipulation and with little danger of introducing infection.

4. *Braxton Hicks' version* was introduced in 1864, at a time when the expectant treatment for placenta previa resulted in a terrific mortality and the new technic represented a distinct advance in therapy. The method gained its greatest popularity before cesarean section became a safe procedure, and its use has decreased steadily with the increasing safety of abdominal delivery. The method, when successfully carried out, controls further hemorrhage effectively. The baby's body exerts adequate pressure against the placenta and lower uterine segment, providing some traction is applied to the delivered leg.

Experience has emphasized several precautions that must be taken with this method. In the first place, following the completion of the version, no attempts at

delivery must be made and a spontaneous delivery must be awaited. The only manipulation justifiable is the maintenance only of sufficient traction to control bleeding. In Hauch's statistics, Braxton Hicks' version alone without extraction resulted in a maternal mortality of 11.7 per cent; where version was subsequently followed by extraction the mortality almost doubled, 20 per cent. The increased mortality is due to serious lacerations of the cervix and lower uterine segment when the fetus is delivered through an incompletely effaced and dilated cervix. The abnormal attachment of the placenta results in a pathologic vascularization of the lower uterine segment and cervix, so that this normally elastic, tough tissue tears at the slightest manipulation, opening up enormous sinuses. This pathologic vascularization and loss of integrity on the part of the lower segment makes other methods of surgical delivery through the natural passages equally hazardous.

The procedure is a difficult operation for the relatively inexperienced physician to carry out successfully with a minimum amount of trauma and blood loss. Version, when dilatation is sufficient to introduce the hand, may be difficult, but when it is to be performed through a cervical canal dilated only sufficiently to admit two fingers, when the placenta covers the os and interferes with free intrauterine manipulation, the procedure may be exceedingly difficult. Anesthesia is usually necessary. These and other difficulties encountered are probably responsible for the marked variation in results obtained by various clinics. It is conceivable that the more experience one gains with this method, the better his results will be. Olow of Stockholm reported a maternal mortality of 9.3 per cent; Essen-Möller 7.6 per cent; Irving has had a decreasing mortality with experience and selection of cases; at the Chicago Lying-In Hospital the author reported a mortality of 1.25 per cent from 1918 to 1927; two of the three maternal deaths resulted from Braxton Hicks' version.

5. *Willett's method* of treating placenta previa is worthy of note. The procedure consists of obtaining a firm grasp of the fetal scalp by means of a modified vulsellum forceps and using this means of applying steady and continuous traction of the head. The illustration demonstrates the principle of the method. Willett's forceps are ideal for this purpose; however, a long, heavy vulsellum forceps can be substituted. The presenting part can thus be kept closely applied to the placenta, thereby controlling the bleeding. Dilatation of the cervix with normal delivery of the infant is awaited.

Although living children have been delivered by this procedure, it is preferable to confine its use to previable infants. Properly carried out, it is effective in arresting the blood flow. This method should largely replace Braxton Hicks' version in marginal and partial degrees of placenta previa because of its simplicity and the technical difficulties of the latter procedure. Should an emergency arise in the home, Willett's procedure could be carried out with a minimum of manipulation and experience. The method has had considerable vogue in Great Britain but it has been rarely made use of in America.

6. Mäurer in 1887 introduced *metreuryosis* in the treatment of placenta previa. This method gained considerable popularity through the work and writings of Dührssen. The idea of introducing a rubber balloon into the lower uterine segment and distending it with some fluid medium to exert pressure appears at first hand to be a good one. The bag should be introduced intraovularly, after rupture of the membranes. Properly introduced it serves to compress the placenta against the uterine wall, effectively controlling further hemorrhage. A bag of 10 or 11 cm. in diameter across the base should be used, so that sufficient dilatation for immediate delivery is obtained on its passage. Sufficient traction should be applied to the bag to keep it closely applied to the placenta. A weight of 250 to 500 gm. attached to the bag and suspended over the end of the bed or over a pulley is usually effective. The passage of the bag is rarely followed by spontaneous delivery so that recurrent bleeding may necessitate delivery by version and extraction or by forceps.

The practical objections to this method are the following: The progress of the bag in securing dilatation must be carefully followed. Immediately after it has left the cervix it must be removed from the vagina so that it does not act as a plug behind which serious hemorrhage may occur. The passage of the bag may have to be followed by further manipulation for the delivery, thereby adding to the danger of trauma and infection. The foreign object introduced into the uterus, and often left in situ for twenty-four hours and longer, increases the incidence and hazards of infection, always a real danger in placenta previa. Sudden expulsion of the colpeurynter may result in extensive lacerations with serious hemorrhage. Last, a suitable rubber balloon may not always be available.

In that many women who were treated by metreuryesis to control the hemorrhage, subsequently had other obstetric procedures to complete delivery, it is difficult to collect statistics for the former operation alone. Hauch in his survey of Danish cases reports a maternal mortality of 12 per cent; Olow of 7.5 per cent for Sweden; Peckham of Johns Hopkins Hospital, where metreuryesis predominated in the treatment of placenta previa, reported a mortality of 8.64 for the last ten years preceding 1930. It is of interest to note that this procedure offers a better prognosis for the baby than does the operation of Braxton Hicks' version, where the baby is most often sacrificed as a tampon to control the mother's bleeding.

7. A new epoch in the treatment of placenta previa began with the introduction of *cesarean section*. The first abdominal section for this condition was performed in this country by Houston Ford in 1892. Dudley published an article in 1900 and stated that "cesarean section is the ideal treatment of placenta previa." In England this operation in placenta previa was taken up by Lawson Tait; in France by LePage; in Germany by Krönig and Sellheim in 1908. Cesarean section during these early years carried a considerable mortality even though uncomplicated by placenta previa, but in spite of this the results obtained were considerably better than with the older methods of treatment. The use of cesarean section spread slowly throughout Europe, but very rapidly in this country.

8. *Vaginal cesarean section* had considerable vogue in Germany. The method rapidly lost its popularity because of the associated high mortality. The advantage offered by this operative route, because of the decreased danger of infection, was lost in the increased danger of serious hemorrhage. All operative manipulations on the cervix and lower uterine segment, the seat of a placenta, are extremely difficult and hazardous. Hauch in his collected statistics reported a mortality of 24.1 per cent; Olow 10.1 per cent. This method has not been used extensively in any of the American clinics.

9. With the introduction of the *low or cervical cesarean section* and its increased safety, the use of abdominal delivery in the treatment of placenta previa has gained tremendous impetus. The Eighth Congress of the French obstetricians and gynecologists in 1933 carefully considered the results obtained in the treatment of placenta previa in the leading clinics of the world and concluded that abdominal cesarean section was the treatment of choice in all serious cases of placenta previa. Similar conclusions were reached by the Northern Surgical Society in Stockholm in the same year, representing Norway, Sweden, and Denmark; Essen-Möller in 1934 concluded that abdominal cesarean section was justified in all serious cases. In Germany, Mikulicz-Radecki expressed similar views.

In the United States, DeLee was the first to advocate more widespread use of low or cervical cesarean section or laparotrachelotomy in placenta previa. Bill of Cleveland extended its use to include all types of this condition. Irving, at the Boston Lying-In Hospital, has steadily increased the incidence of cesarean section in placenta previa. Johns Hopkins was the last large clinic to adopt this treatment in selected total placenta previa cases, although Williams was never thoroughly convinced that this was ideal treatment.

Theoretically, cesarean section offers many advantages in the treatment of placenta previa. The low or cervical operation invades the placental site, and although considerable bleeding may occur the entire bed of the placenta is open to inspection. Bleeding can be controlled by careful packing and suturing. Although it is rarely necessary, a bleeding sinus can be stitched. The pathologic uterine wall is not traumatized, thereby minimizing the likelihood of infection. In some cases where the placenta is attached to the anterior wall of the lower segment, necessitating extensive laceration of the placenta before the uterine cavity is entered, a low classic section may be preferable. Some authors advocate the routine use of the classic section for placenta previa, thereby avoiding the placenta and its site. The greater security of the low operation from postoperative complications, however, usually outweighs the increased difficulties encountered in its performance in placenta previa.

Although the low or cervical cesarean section provides considerable safety from infection, its use in the obviously infected case is not advisable because of the likelihood of a serious extension. Patients who present themselves with obvious infection as a result of previous manipulation, packing, or mismanagement, had better be treated by conservative methods. Porro cesarean section, or cesarean section followed by hysterectomy, has received increasing popularity in these cases. Many patients are multiparas, when the operator need not be too greatly concerned by the sacrifice of the uterus. The careful surgical removal of the large infected uterus, often the focus from which the general infection develops, results in a decreased incidence of serious, postoperative puerperal infection.

The maternal mortality of cesarean section in the treatment of placenta previa differs greatly, and is largely determined by the cesarean section mortality of the clinic and the class of patients treated. At the Chicago Lying-In Hospital we have delivered 120 patients with serious degrees of placenta previa without maternal mortality. Bill of Cleveland has reported equally good results. Large series of cases have been reported in which the mortality is as high as 10 per cent; Hauch's was 9.7 per cent; Pankow's 4.4 per cent. The maternal mortality is largely the result of a general infection superimposed on a patient so seriously depleted of blood that she offers little if any resistance.

TABLE I. CHICAGO LYING-IN HOSPITAL STATISTICS
JANUARY, 1927, TO JANUARY, 1936

<i>190 Cases of Placenta Previa</i>		
MARGINAL 99	PARTIAL 25	TOTAL 66
<i>Methods of Treatment</i>		
	NO. OF CASES	PERCENTAGE OF CASES
Low or cervical cesarean	80	46.5
Porro cesarean	8	
Vaginal cesarean	1	
Rupture of membranes	32	16.8
Metreuryxis	28	14.7
Braxton Hicks' version	23	21.1
Breech extraction	8	4.2
Forceps delivery (only)	11	5.7
<i>Mortality</i>		
MATERNAL	FETAL	
None	Total	64 or 33.6%
	Previa and monstrosities	48
	Viable normal	16
	Corrected mortality	8.4%

PRINCIPLES OF TREATMENT

In the preceding brief résumé of the various treatments advocated in placenta previa, the tendency toward a more rational therapy can be noted. No one method offers the ideal solution for every case because of the many factors involved, such as the degree of placenta previa, the patient's condition, her parity, the duration of the gestation, the patient's environment, and the attendant's skill. These and other variable factors influence greatly the therapy and its ultimate result. Thus we see that in spite of an accumulated experience of years in thousands of cases, our collected results still warrant improvement. Munro-Kerr reports that the maternal mortality in England and Wales is 14.11 per cent; in Scotland 11.9 per cent; the U. S. Children's Bureau reported that 11 per cent of maternal deaths resulted from hemorrhage. According to the 1934 Report on Maternal Mortality in Philadelphia, 8.7 per cent of the deaths resulted from placenta previa.

In recent years the importance of other factors than the mode of delivery has been repeatedly emphasized. Early recognition and treatment of the condition, hospitalization, proper preparation of the patient before delivery, and free use of blood transfusion are probably of equal importance as the method of delivery.

The ideal management of placenta previa should begin in the prenatal period. The patient's history should include information concerning any hemorrhage in previous pregnancies. The patient should have a careful blood study. Anemic patients should receive adequate therapy during the pregnancy for the restoration of the normal blood picture. There has been an increase in the anemias of pregnancy during the last economic depression. At the Chicago Lying-In Hospital 12 per cent of pregnant women had a hemoglobin of less than 10 gm. per 100 c.c. of blood. Patients with a very low hemoglobin should be transfused before delivery. It requires little discussion to emphasize the fact that the anemic patient will withstand a moderate blood loss poorly and a serious blood loss not at all. To carry modern prenatal care a step further, the doctor in the smaller community where medical facilities may be somewhat limited, particularly in an emergency, would do well to determine the patient's blood group. In this age of prophylactic medicine he can even go a step further and group and match the husband or some other members of the family. Thus, when an emergency arises, a safe blood donor is immediately at hand and precious minutes are saved. Fewer serious mistakes will be made under the stress of pressing events.

Bleeding during pregnancy at any time must be considered abnormal and of sufficient importance to warrant investigation. Patients must be taught to report any bleeding occurring during gestation. When the bleeding occurs during the last trimester of pregnancy, it should be regarded of sufficient import to merit an examination, in a hospital if possible. In the literature which has been reviewed, several impressions stand out vividly. In the first place, placenta previa is a complication necessitating hospitalization. Only under unusual circumstances is it justifiable to treat a patient in the home. In the second place, women should be referred to a hospital with their initial bleeding without manipulation in the home. To obtain any improvement in our results, these two fundamental principles must be observed.

The initial hemorrhage in placenta previa is rarely alarming. The characteristic course is small, repeated hemorrhages, and finally a serious hemorrhage. These small hemorrhages are the warning signs of a serious calamity. The patient should be referred to a hospital for diagnosis and treatment at the first sign of bleeding in the last trimester. This regime will rarely necessitate examination in the home with its possible complications.

Examination of bleeding cases in the home is always fraught with danger. A simple examination for diagnosis may stir up a profuse hemorrhage necessitating further manipulation for its control. Packing for the control of bleeding adds

greatly to the danger of infection and is often ineffective in controlling the bleeding. These manipulations for diagnosis and control of hemorrhage often alter the subsequent course of treatment and make a favorable prognosis unfavorable. The patient who is referred to a hospital at the earliest sign of bleeding will rarely be jeopardized by the transportation, if she has not been previously examined.

The maternity department of every hospital should have a smoothly functioning regime for the treatment of bleeding cases. Indeed, in some of the foreign countries, special centers have been set up for the treatment of patients bleeding in pregnancy, in an effort to lower the high maternal mortality. The patient, on entering the hospital, should have her blood group determined and her blood should be cross-matched with that of a suitable donor. Examinations of all kinds are usually postponed until a donor is available, for once an examination is done, the appropriate therapy must be instituted. The patient who has lost considerable blood and shows the general effects of the blood loss should have a preparatory transfusion. This will fortify her against an unusual blood loss during the subsequent diagnosis and treatment. Bill first pointed out the value of this procedure, which we have adequately confirmed at the Chicago Lying-In Hospital.

Before the vaginal examination is started, preparations should be completed for obstetric procedures from below or possible cesarean section. The degree of previa is determined as well as the state of the cervix, the size of the pelvis and the maturity and size of the fetus. We distinguish clinically, *marginal placenta previa* where the edge of the placenta is palpable at the cervical os, *partial placenta previa* where a portion of the os is covered by placental tissue, and *total placenta previa* where the entire os is covered by placenta. The degree of placenta previa is determined when the patient is first seen, irrespective of the dilatation of the cervix. In that most cases are examined and treatment instituted before the advent of labor, it is not feasible or necessary to determine the placental location more accurately. The maturity of the fetus is estimated, and its extrauterine viability considered for this may effect the procedure to be followed. The examination concluded, appropriate treatment is instituted depending on the exigencies of the case.

It is rarely desirable to postpone the termination of pregnancy in placenta previa. The initial hemorrhage is usually followed by repeated bleedings, any of which may seriously endanger the patient's life. With the slow development of the lower segment more and more placenta must be separated from its attachment and hemorrhages will continue. The presence of blood in the vagina predisposes to infection by a change in biologic relationships. Necessary subsequent manipulations become more hazardous in the presence of a virulent bacterial flora. These real dangers make the policy of "watchful waiting" for viability of the baby undesirable, except under unusual circumstances, and then only with the patient most carefully observed in a hospital. This policy must result in a necessary sacrifice of previable fetuses.

The treatment instituted will depend on the many factors previously discussed. Marginal placenta previa and partial placenta previa in multiparas in good condition can best be treated by simple rupture of the membranes. Where this does not control the bleeding, one of two procedures can be instituted: Braxton Hicks' version or metrenrysis. Where the fetus is previable, a careful Braxton Hicks' version is probably the treatment of choice, although its performance may be difficult. The use of Willett's method should be considered. The careful intraovular introduction of a suitable bag, large enough to provide sufficient dilatation on its passage, is preferable where the fetus is viable. It is probably a more simple procedure than Braxton Hicks' version but demands more careful and intelligent observation for a satisfactory result. Following the passage of the bag through the cervix, a spontaneous delivery can be awaited if there is no bleeding, or delivery can be accomplished by version and extraction, or when the head is engaged, by forceps.

The management of the third stage of labor is worthy of some comment. Following the delivery of the baby, normal separation of the placenta can be awaited unless bleeding occurs. In that event careful manual removal is indicated. In the event a difficult operative procedure has taken place, a careful examination of the entire lower uterine segment and inspection of the cervix for lacerations should be instituted. Lacerations which cause bleeding should be repaired. Atony of the uterus following placental expulsion necessitates careful exploration of the uterine cavity, evacuation of clots, and oxytocic drugs. If the bleeding continues, the uterine cavity should be firmly packed, packing the corporeal cavity first and then the stretched, traumatized, bleeding lower segment, and finally the entire vagina. An insecure or improperly placed pack is worse than none at all, for it acts as a plug behind which bleeding continues. It is good practice to administer pituitary extract intramuscularly or better yet, ergonovine intravenously, just as the baby is being delivered, thereby hastening the third stage.

Cesarean section should be reserved for the patient with total placenta previa; in the partial placenta previa when the placenta covers a considerable portion of the cervical os and the patient is a primipara; any patient that enters the hospital exsanguinated and in critical condition; where some other indication than the placental location exists, such as a borderline pelvis or an elderly primipara. The low or cervical cesarean is probably the preferable procedure unless the placenta is palpated during operation on the anterior wall, then the low classic is probably the simpler procedure. Porro cesarean should be considered in early multiparas with partial or total placenta previa, who are grossly infected due to previous manipulation.

It cannot be too strongly emphasized that measures for combating blood loss are a most essential part of any treatment of hemorrhage in pregnancy. The subsequent maternal mortality, serious puerperal infection, and prolonged convalescence and invalidism can be greatly reduced by a serious attempt to restore in some measure the blood loss of the patient. For maintaining blood volume, saline or Ringer's solution can be given by hypodermoclysis, using 16 gauge needles. Glucose solution in 20 per cent concentration should be given intravenously at as slow a rate as possible, discontinuing its administration just as soon as blood is available. No more than 500 c.c. should be given unless a liberal blood transfusion follows. It must be remembered that large amounts of hypertonic glucose solution draw liberally on the fluids in the tissues and increase blood coagulation time. In the event blood is not immediately available 500 to 1,000 c.c. of 6 per cent acacia can be slowly administered intravenously. Although the blood volume be restored, sufficient circulating hemoglobin must be present to carry on the vital functions of life. The amount of the transfusions should depend on the blood loss, averaging 600 to 800 c.c. in the usual case. Dieckmann and Daily report that in 22 cases in which the blood loss was measured it averaged 824 c.c., and these patients received a total of 29 transfusions averaging 670 c.c. of blood per patient.

Throughout this discussion little has been said concerning the interests of the baby in the management of placenta previa. This condition is a maternal complication and of such serious import that the mother's interests must be considered first and guarded always. The baby's interests must always come secondary in any decision. The treatment which assures a living baby and at the same time safeguards the mother's life is certainly to be preferred.

Placenta previa carries with it an inevitable fetal mortality. This condition frequently manifests itself so early in the course of the gestation that the baby could not carry on an extrauterine existence regardless of the method of delivery. In our series 10 per cent of the pregnancies were terminated before the thirtieth week, and these previable fetuses had no chance at survival; another 10 per cent were terminated before the thirty-fifth week with only a fair chance at survival. Some of the

fetuses succumb as a result of separation of the placenta and a deficient circulation, others become exsanguinated by traumatic lacerations of the placenta as a result of operative manipulations, but the majority sustain fatal injuries during their delivery.

That the fate of the infant depends largely on the method of treatment can be seen from the following figures. When the treatment consisted of rupture of the membranes, the gross fetal mortality was 33 per cent; metrorrhysis, 50 per cent; Braxton Hicks' version where the infant must of necessity be disregarded, 54 per cent; in cesarean section, 12 per cent. Thus, it is brought home to us that cesarean section safeguards the interest of the baby the most. By this method many babies at the borderline of viability are delivered uninjured and take up a normal extra-uterine life. The tremendous increase in the safety of the baby given by this method over other methods in vogue has been a powerful argument used by many clinicians who propose to widen the scope of this treatment. The ever decreasing size of the family has resulted in an ever increasing value of the unborn baby.

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Berger, Louis, Vallee, A., and Vezina, C.: Genital Staphylococcic Actinophytosis (Botryomycosis) in Human Beings, *Arch. Path.* 21: 273, 1936.

True botryomycosis, a veterinary pathologic entity found in the horse, cow, sheep, and pig, is only very rarely seen in the human being. In the botryomycotic lesions, the organisms were supposed to be mycotic elements akin to actinomyces. It was later demonstrated that botryomycotic lesions are of a staphylococcal nature. Until this case appeared, there were only four cases of this sort reported in man, all associated with osteomyelitis. The patient was a woman aged fifty-three, with a tumor in the posterior part of the left labium majus. The tumor increased in size and a specimen was removed for biopsy and cultures made. The culture showed *Staphylococcus aureus* and *B. coli*. The process persisted for twenty months and resisted all forms of treatment, including x-ray. The lesions were inflammatory and were identical with those described in animals. The coexistence of *B. coli* within the granules was a heretofore unknown feature.

W. B. SERBIN.

Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK

Review of New Books

Obstetrics

*Antenatal and Postnatal Care*¹ is a concise, practical, and substantial book, written with the purpose of providing, in the author's words, "instruction in the more recent advances in antenatal care and . . . the methods used in its practice," and presenting specifically the teaching of the University College Hospital in London. The book covers its field adequately, including chapters on the history and development of antenatal care, the clinic and its equipment, examination of the patient, the diagnosis of early pregnancy, hygiene of pregnancy, influence of the emotions on pregnancy and parturition, maturity, and postmaturity with more or less special reference to forensic medicine, abnormal presentations and positions, multiple pregnancy, abnormalities in the quantity of amniotic fluid, hemorrhage in early pregnancy, antepartum hemorrhage, contracted pelvis and disproportion, uterine displacements and pregnancy, vomiting in pregnancy, preeclamptic toxemia and eclampsia, disorders of the digestive, circulatory, nervous, endocrine, respiratory, and urinary systems during pregnancy, affections of the skin in pregnancy, tumors complicating pregnancy, labor and the puerperium, venereal diseases in pregnancy, and postnatal care. There are in addition six appendices including sample clinic record sheets, technique for medical induction of labor, diets, and a discussion of the conduct and scope of antenatal clinics. There are also an excellent bibliography and a fairly complete index. The book is well illustrated.

Representative chapters on the important topics of placenta previa, contracted pelvis and disproportions, vomiting in pregnancy, and preeclamptic toxemia and eclampsia are of particular interest. For placenta previa, or suspected placenta previa, the author advises conservative treatment, excluding even vaginal examination in the hospital if the bleeding is slight and the patient not in labor. For more severe bleeding, the active treatment familiar in this country is recommended, including full preparation for immediate transfusion and cesarean section before a vaginal examination in the operating room is done. Cesarean section is the treatment of choice if the os does not admit a finger; if the os admits two fingers and the placenta completely covers it; if a live child is particularly desirable, as in elderly primiparae; in the presence of disproportion or other serious complication; in patients treated expectantly in whom there is evidence that the placenta overlaps the internal os, the section being done as soon as the patient reaches the thirty-sixth week of pregnancy; and occasionally in patients whose condition is so critical that vaginal manipulation is deemed likely to cause a further fatal hemorrhage. In the cases not treated by cesarean section the choice may include Willett's scalp traction forceps with 1.5 pounds weight attached, pressure by the half breech on the bleeding point, rupture of membranes and tight binder, but never the De Ribes' hydrostatic bag.

¹*Antenatal and Postnatal Care*. By Francis J. Browne, M.D., D.Sc., F.R.C.S. (Edn.), F.C.O.G. Professor of Obstetrics and Gynecology, University of London, etc. With 58 illustrations and 480 pages. J. and A. Churchill, Ltd., London, 1935.

Contracted pelves are classified strictly after Caldwell and Moloy, treatment taking the form of cesarean section, trial labor, or induction of premature labor. Section is advised if the conjugata vera is under 3.25 inches in a flat, or 3.5 inches in a generally contracted pelvis and in most elderly primigravidas with contracted pelves unless there is no disproportion. With respect to trial labor the author says, "A fair trial of labor can only be said to have been given when good pains have been recurring every four or five minutes for at least two hours, during which the cervix has been fully dilated and the membranes ruptured." As the author points out, "induction of premature labor for contracted pelvis is a peculiarly English method of treatment, and has never found much favor in American or continental clinics." Labor is induced after the thirty-fifth week, following a sterile vaginal examination, by instrumental means as a rule. Gum elastic bougies, stomach tubes, hydrostatic bags, balloons, or glycerin-filled animal bladders are generally used. Artificial rupture of the membranes is not allowed.

Vomiting in pregnancy is resourcefully discussed, the methods employed in treating true hyperemesis gravidarum apparently differing little from those used in this country, although the indications for termination of the pregnancy are perhaps slightly less exacting. Emphasis is placed on the importance of liver damage in this condition, and jaundice of a mild degree, or even slight bilirubinuria is regarded as a grave prognostic sign.

The management of pre-eclamptic toxemias and of eclampsia also accords in general with the usual view in America. Early recognition of an impending toxemic state is stressed, as would be expected in a book on prenatal care, but a full discussion of the whole topic of toxemias is given, the author endorsing the opinions of Stander and Peekham regarding the outlook in chronic nephritis.

Dr. Browne's book is readable, well informed, and discriminating in its dogma. It is a contribution of importance in a still somewhat neglected field.

FRED L. ADAIR.

*Abortion, Spontaneous and Induced*² by Taussig is a most important contribution on this subject. It is one of a series dealing with medical aspects of human fertility sponsored by The National Committee on Maternal Health. The purpose of the book is to help the practitioner and specialist in the diagnosis and treatment of abortion, as well as to inform the sociologist and student of public health of the facts necessary to understand the way in which abortion undermines the physical well-being and moral integrity of the community.

The statistics on abortion, no matter how carefully compiled, are inaccurate. Taussig, after most thorough study of the world literature, concludes that 1 abortion occurs in every 2½ confinements. This signifies some 680,000 abortions annually in the United States, of which approximately 4,000 prove fatal. An interesting chapter of the book is devoted to abortion in animals by W. L. Williams. In the cow and in the mare abortion can be induced by squeezing out the corpus luteum through the rectum. Causes for abortion in animals, and this plays a huge economic rôle in every country by reducing the fertility of herds, can occur through too frequent coitus, by the covering of too young animals, and particularly in goats, sheep, and swine through the *Bacillus abortus*. In cows, Williams is by no means sure that the bacillus plays as great a rôle as has been ascribed to it. Here the venereal infection of cattle is most important.

Only the briefest survey of the contents of this book of 536 pages can be given. The author discusses the anatomy and physiology of early pregnancy, the pathology of abortion, the causes of spontaneous abortion, both ovular and maternal, the

²*Abortion, Spontaneous and Induced. Medical and Social Aspects.* By Frederick J. Taussig, M.D., Professor of Clinical Obstetrics and Gynecology, Washington University School of Medicine, 536 pages. Illustrated. The C. V. Mosby Co., St. Louis, 1936.

exciting causes. In the discussion of the prevention of abortion, I note that no mention of progestin is made. Taussig advises extremely conservative treatment of septic abortion. He approves, however, of the emptying of the uterus if the temperature has remained normal for three to five days, then advises delayed emptying. Perforation and other complications of induced abortion are described in detail. The indications for therapeutic abortions are thoroughly entered into and the author's point of view is sane and conservative, particularly in abortion for tuberculosis where he emphasizes that economic reasons must be fully considered as tuberculosis is such a long-drawn-out disease. The technic of abortion is likewise dealt with.

The chapter on statistics on abortion throughout the world is of great interest and importance. The theological and ethical aspects of induction, a full description of legalized abortion in the Soviet Union where the mortality is only 1/100 of that of the German rate, which of course includes clandestine abortions in that country, is included.

The final chapter deals with the legal aspects of induction of abortion in various countries and states, as well as a summary of the statutes relating to abortion in the various states of our Union.

The book is copiously illustrated. The line drawings are faultless while for some reason many of the half-tones are reproduced in a rather flat fashion. This book is to be highly recommended to the medical profession and to others interested in sociologic conditions.

R. T. FRANK.

Based upon his method of teaching for some years in the Harvard Medical School, Irving presents *A Textbook of Obstetrics*,³ moderate in size and clear and concise in text. The book may be accepted as representing the policies and practice of the Boston Lying-In Hospital of which the author is visiting obstetrician.

The book is divided into two parts, Normal Obstetrics, and Abnormal Obstetrics. The first carries the reader logically through anatomy, normal pregnancy, its physiology, changes, hygiene, and necessary antepartum studies. The physiology of labor and the mechanisms of the various presentations follow. There is a discussion of the physician's part in labor, a description of the involutational period changes, lactation and a final chapter on the newborn, discussing the sick and injured infant, written by S. H. Clifford.

Under Abnormal Obstetrics, the author discusses pathology of pregnancy, the pathology of labor, the dystocias, and the accidents of parturition. Obstetric surgery defines and describes the various operations of delivery and reconstruction. The pathology of the puerperium takes up specific puerperal infections as well as other diseases common in the puerperium. The book closes with an appendix of x-ray photographs. There are over 357 illustrations which are well chosen to correlate with the text; a large proportion apparently come from other works. A noteworthy feature of the book is an excellent bibliography following each chapter.

The physiology of conception gives a most recent review of the interglandular hormonal relationship. The influence of these hormones is further discussed in the section on the growth of the fetus and again in the chapter on hygiene of pregnancy. The author emphasizes weight estimation in pregnancy as an index of toxemia, later in the book he refers to excessive weight gain in pregnancy as frequently followed by inertia uteri during labor although he does not explain the correlation. The recent studies of Caldwell and Moloy on the obstetric pelvis are described, and the author gives a very simple classification, later on, of contracted pelves. The

³*A Textbook of Obstetrics. For Students and Practitioners.* By Frederick G. Irving, M.D., Professor of Obstetrics, Harvard Medical School; Visiting Obstetrician, Boston Lying-In Hospital. 558 pages. The Macmillan Company, New York, 1936.

mechanical principles and processes involved in different presentations are well presented, and explained by accompanying black and white sketches.

The author feels that many labors can be conducted with rectal examinations alone. He states that vaginal examinations should be made only when the derived information will prove of benefit to the patient. In the chapter on conduct of labor is a discussion of obstetric anesthesia, the mode of action and the administration of various agents. The author indicates a preference for pentobarbital in combination with scopolamine which, he states, should never be used in the private house on account of the considerable excitement it sometimes produces. He does not, however, suggest a satisfactory substitute for domiciliary practice. Statistically the results of barbiturates in his hands have been unusually satisfactory since there were no failures from the standpoint of amnesia. Under asphyxia the author regards the use of carbon dioxide for resuscitation as irrational based on the finding that the carbon dioxide tension in asphyxia is almost twice that found in normal infants.

The author is conservative in his handling of abortion complicated by fever, refraining from interference except for hemorrhage or well-defined sapremia. All infants weighing five pounds, or less, in the Boston Lying-In Hospital are considered as premature, even though they are born at the expected date of confinement. Low forceps delivery of premature infants is favored as followed by a lower fetal mortality than spontaneous deliveries.

The subject of placenta previa is thoroughly discussed. Under treatments the author has favored conservative measures with vaginal delivery with resulting high fetal mortality and states that a more liberal indication for cesarean section in this condition may be his future plan. In premature separation of the placenta he has had excellent results with rupture of the membranes, the Spanish windlass abdominal binder, and pituitrin.

The author considers three toxic conditions, nausea and vomiting, preeclampsia, and eclampsia. He advises conservative treatment of hyperemesis, but gives very definite indications for interruption of pregnancy. The author does not accept the term low reserve kidney and substitutes a new classification of toxemia from his own clinic. In discussing the termination of pregnancy in preeclampsia there is a rather ambiguous statement as to mortality of cases delivered by cesarean section, which might seem to demand revision. The author devotes considerable space to the pathology and morbid physiology and theories of eclampsia. The treatment recommended is conservative and includes a procedure, plasmapheresis, which the bibliography of the chapter would seem to indicate had not been widely copied.

The section of the Diseases of Circulatory Symptoms written by B. E. Hamilton is an excellent recapitulation of the splendid work done on heart diseases and pregnancy in the Boston Lying-In Hospital.

In the consideration of the contracted pelvis stereoroentgenometry of the head is favored, and there is little mention of pelvic roentgenometry.

The section on operative obstetrics describes in full with explanatory illustrations the technic favored in the author's clinic. Cervical lacerations are repaired only for hemorrhage. The operation favored for posterior position of the occiput is not recommended for other than experienced operators. The high forceps operation has disappeared, statistically. The operation of breech extraction is evidently limited to definite indications and is well illustrated. The author describes and illustrates the technic of various types of cesarean section; he states in Massachusetts one out of every ten women who dies from childbirth causes loses her life following a cesarean section. In the consideration of puerperal infection he favors a generally conservative treatment and feels that there may be some hope in the use of Lash's antistreptococcus antitoxin.

This is a very clear and concise presentation of the author's teaching. The subject has been entirely covered in a pleasant manner. There is enough theory

to interest a student, and there is plenty of conservative treatment outlined for the practitioner. The principles and practice elaborated are evidently those which have been thoroughly tested in the mill of a busy obstetric clinic, and on the whole the book deserves a very hearty commendation.

PHILIP F. WILLIAMS.

Devraigne presents in his *Cliniques Obstetricales*⁴ some lectures which he has given at the Clinique Baudelocque to students and graduates. These lectures published in different journals have been gathered and present in a collective form various topics of the pathology of pregnancy, dystocia, and the therapeutics of obstetrics in order to emphasize particular points, largely of a practical nature.

There are nineteen subjects handled in this volume which opens with a discussion of prenatal hygiene. Devraigne discusses the subject more from the standpoint of state care of women in relationship between the consulting physician at the prenatal clinic and the practicing midwife in the district, and mentions the importance of having a physician supervise antenatal care notwithstanding the midwife is to be in charge at the time of delivery.

The second lecture is on obstetrical diagnosis and there are three lectures on abnormally situated pregnancies and one on the anomalies of the position of the uterus. Hyperemesis gravidarum, diabetes, colon bacillus infections and pyelitis are well handled. The suggestions as to treatment are much in accord with American practice. In discussing hydatiform mole, he stresses a continuing hormone study of the individual. There are two papers on rupture of the uterus. He refers to the advisability of spinal anesthesia as the most favorable relaxing agent for those circumstances which necessitate rapid vaginal delivery. The indications of low cervical section form the basis of the next paper on dystocia and complications of labor.

The subject of puerperal infection particularly from the bacteriologic standpoint is reviewed under the title of puerperal scarlatina in which reference is made to much of the American work on the streptococcus and scarlet fever. In the concluding lecture he describes treatment of puerperal infection in its general and specific applications, in which he lays stress on protein shock therapy by intravenous injections.

This interesting collection of clinical talks constitutes a current French viewpoint on important obstetrical subjects.

PHILIP F. WILLIAMS.

In the introduction of this the fourth edition of his *Lehrbuch der Geburtshilfe*,⁵ Jaschke mourns the death of his former co-author, Otto Pankow who had contributed in the previous editions, physiology and pathology of labor and the pathology of the puerperium.

The volume is a fine example of German bookmaking. There are 573 beautifully drawn illustrations, a great many of which are colored either in whole or in part.

The new material of the physiology and biology of pregnancy has been thoroughly covered in this edition and especially as regards sterility and fertility. In the preface to the book reference is made in a footnote to the fact that the birth rate in Germany since the first half of 1934 has shown a slight upward tendency and the number of abortions have perceptibly declined, phenomena which Jaschke attributes to the influence of National Socialism.

⁴*Cliniques Obstetricales*, par L. Devraigne, charge de cours de clinique annexe de la faculté de médecine de Paris. 240 pages, G. Doin & Cie, éditeurs, Paris, 1936.

⁵*Lehrbuch der Geburtshilfe*. Von Dr. Rud. Th.v. Jaschke. Vierte Auflage, mit 573 zumteile farbigen Abbildungen. 770 Seiten. Verlag von Julius Springer, Berlin, 1935.

In rewriting the chapters on the physiology and pathology of birth, von Jaschke makes excellent use of roentgen ray pictures of different stages of labor in both normal and abnormal pelvis and in abnormal positions of the fetus. His illustrations adapted from Sellheim's phantom do much to clarify the mechanism of birth. At the present time the Giessen Clinic prefers pernocton as a means of obstetric amnesia-analgesia. The toxicoses of pregnancy are very fully discussed. For hyperemesis gravidarum, von Jaschke uses intravenous glucose, for convulsive toxemia the Stroganoff technic.

The section on operative obstetrics is most complete and beautifully illustrated. The low cervical section recommended follows the technic of Opitz. The chapter on puerperal sepsis and other conditions of the puerperium previously contributed by Pankow has been entirely rewritten. Von Jaschke describes various types of puerperium infections as he differentiates them pathologically. He recommends conservative medical therapy, transfusions, nonspecific protein therapy, and surgery indicated only for localized abscesses. He places little reliance on dyes or other chemicals applied intravenously.

This very fine example of obstetric teaching in Germany may well be regarded as a reference book of unusual worth.

PHILIP F. WILLIAMS.

Miscellaneous

The title of this impressive work is *Woman*,⁶ an historical, gynecological and anthropological compendium. Compendium seems a rather modest description of this encyclopedia presented in three large volumes, which comprise more than 2,000 pages and contain more than 1,000 illustrations.

In 1846, Heinrich Ploss received from the University of Leipzig the degree of *doctor medicinae* on a thesis entitled: "The Origin of Psychoses in the Puerperium." A few years later he began to specialize in obstetrics and published many papers dealing with various obstetric questions. His special interest in ethnologic and anthropologic problems he first manifested in 1870 in a paper on the different methods employed by various peoples in severing the umbilical cord. There followed in short succession, within a year or two, several papers describing: peculiar alterations of the external genitalia by means of mutilating, ceremonial operations; differences in pubic hair among different races; the varying practices of disposing of the placenta, etc. Ploss published in 1884 a small volume entitled: "The Child, in the Custom and Common Usages of Peoples and Races the World Over." In the following year appeared the first edition of the work here reviewed, the renowned *Das Weib in der Natur- und Voelkerkunde*. It was the first exhaustive study ever attempted of woman from the viewpoint of history, ethnology, anthropology as well as obstetrics. In the preface to this first edition Ploss wrote: "I looked upon woman in regard to all her psychologic and somatic characteristics with the eyes both of the anthropologist and the physician." The end of the year 1885 saw Heinrich Ploss's death. The success of his book was truly amazing. Within one year the entire first edition of 1,500 copies had been sold out so that Dr. Max Bartels had to be entrusted with the preparation of the second edition which in thoroughly revised and greatly enlarged form appeared in 1887. Ever since, among the German-speaking profession, this work has been known simply as "Ploss-Bartels." Its unique value as the best and richest source for information on any question pertaining to woman accounts for its wide popularity which has persisted and

⁶*Woman*. By Hermann Heinrich Ploss, Max Bartels and Paul Bartels. Edited by Dr. Eric John Dingwall. With more than 1,000 illustrations in black and white and seven color plates. Three volumes, 2,020 pages. The C. V. Mosby Co., St. Louis, 1936.

increased as editions followed each other from the hands of successive editors, always competently reflecting newly obtained information from foreign lands and all recent scientific discoveries.

Though for very many years medical writers in all languages have been in the habit of quoting from Ploss-Bartels, they always had been forced to turn to the German original. Now for the first time an English version (of the eleventh German edition) is offered by Dr. Eric John Dingwall. It would be a hopeless task to outline here the stupendous amount of varied data and fascinating information presented in this monumental work but without exaggeration the assertion can be made that the work in its present form well stands comparison with such classics of scientific literature as Newton's *Principia* or Frazer's *Golden Bough*.

HUGO EHRENFEST.

This book, the first *Textbook on Child Psychiatry* in the English language, is a splendid contribution on a most difficult subject, a beacon light appearing in what many psychiatrists and practically all pediatricians have regarded as an uncharted sea. The author, most fortunately and wisely, has had daily contacts with pediatricians and the personnel of various child-caring agencies, which must surely have aided in broadening his viewpoint and improved his understanding of the child and his problems, physical as well as mental. In consequence, this work will serve as an invaluable reference book to anyone seeking information on the mental processes of youth. But, weighty as the book is in substance (it has 527 pages) and in contents, our fear is that, being written in the complex, highly specialized terminology of the psychiatrist, it may lose a great deal of its appeal to pediatricians and others to whom psychiatry is only one of the specialties about which he is supposed to have a smattering of knowledge. Nevertheless, its casual perusal is an interesting experience, its closer study should prove an important event in the medical life of the average physician. Certainly it belongs in the library of anyone called upon to advise parents in the rearing of their children.

T. C. HEMPELMANN.

The task of reviewing this book is a difficult one. This *Index of Differential Diagnosis*⁸ is a large and forbidding tome of over eleven hundred pages. Your reviewer is prejudiced against indexes, compendiums, and vademecums. An attempt to arrange an alphabetical file for symptoms, or for physical signs, or for treatment has always seemed to him the wrong approach. Anything commendable that the reviewer may say is, therefore, doubly favorable.

In spite of the large number of authors the book has an evenness and uniformity often missing in such collaborations. The fact that the authors are all British may have something to do with this. The British physician can express himself well in the English language. This makes for clarity and easiness of reading.

Some of the objections that an American reader may have to the book are probably based on different attitudes toward the subjects under discussion. Thus there is a long discussion of anemia. This is written by French and makes delightful reading. One is struck by the importance attached to chlorosis. The reviewer wondered how often secondary anemia is due to pyorrhea alveolaris. He missed also any reference to such apparently valid classifications as microcytic and macrocytic or hyperchromic and hypochromic. One who has some knowledge of hematology, and what physician has not, may find the text useful in puzzling situations.

⁷*Child Psychiatry*. By Leo Kanner, M.D., Associate Professor of Psychiatry, Johns Hopkins University. 527 pages. Charles C. Thomas, Springfield, Ill., 1935.

⁸*An Index of Differential Diagnosis* of many symptoms, by various authors, edited by Herbert French, consulting physician to Guy's Hospital. Fifth edition, with 742 illustrations of which 196 are colored, with 1,145 pages. William Wood & Company, Baltimore, 1936.

The subject of jaundice is comprehensively discussed. It is well handled. In mentioning the body fluids that may contain bile the blood serum is not spoken of and no reference made to the icterus index or to the van den Bergh test. One misses any reference to urobilinogen, its ready quantitative determination and its diagnostic importance. Carotinemia is not listed among the conditions that may simulate jaundice.

The pictures, including colored photographs, are, on the whole, good. They add much to the value of the book for one who wants a quick, though often superficial, review of a subject.

The reviewer can recommend the book for one who wants this sort of thing. For those who have access to medical libraries an hour spent there with the standard textbooks and current literature will be more useful.

LLEWELLYN SALE.

The first volume of a new English *System of Post-Graduate Surgery*⁹ edited by Rodney Maingot is an impressive tome of 1,742 pages. The paper is excellent, the print large, the illustrations well executed, and the binding is sturdy. This first volume deals with Anesthesia, The Abdomen, The Rectum, X-Ray Diagnosis, and Radium Treatment.

An American Foreword has been written by Pool and a sentence of it may be quoted: "In this work are presented exhaustive discussions on all branches of surgery carefully prepared and edited; and there is the refreshing aspect that they are transmitted to us from across the Atlantic by many minds with which we are unaccustomed to deal." The book is dedicated to Moynihan, of Leeds, who has written an introduction.

The section on anesthesia has been written by Hewer, and discusses the subject first by agents and their action, and second as to their regional application.

Part Two on the abdomen is edited by Maingot. The papers comprising this part of the book are by a list of notable English surgeons. The medical aspects of abdominal surgery are reflected in several titles as "The Investigation of a Case of Dyspepsia," "Jaundice," "Diabetes in Surgical Cases," "The Spleen and the Blood Platelets." The description and discussion of the Pean-Billroth I operation has been written by Finocchietto, of Buenos Aires, who is the only non-British contributor to this volume. There is a very complete consideration of the surgery of each abdominal organ, with operative technique well illustrated by photographs and diagrams, and with the pathology exposed by photographs and photomicrographs. This part closes with a nine-chapter presentation of the complications of abdominal operations by Maingot, including one by Wright on post-operative phlebitis.

W. Ernest Miles has contributed a section of 222 pages on surgical conditions of the rectum and anus. This is virtually a monograph of the subject. It may be noted that the mortality of the one-stage abdomino-perineal operation for carcinoma of the rectum in his hands has steadily dropped in three successive series from 32 per cent to 17 per cent, and finally to 10 per cent. His five-year salvage, all varieties included, from recent studies shows a survival rate of 69.3 per cent.

Part IV considers the x-ray diagnosis of abdominal conditions. This section, written by Bull, takes up separately the alimentary and the urinary tracts. This discussion, profusely illustrated by skiagraphs and diagrammatic black and white sketches, takes up the diagnosis and differential diagnosis by x-ray of the manifold pathologic processes of the stomach, intestine, and related organs. The congenital and acquired lesions of the urinary system are as thoroughly considered.

⁹Post-Graduate Surgery. Edited by Rodney Maingot, Senior Surgeon of the Royal Waterloo Hospital and Southend General Hospital. Volume I, with 846 figures in the text, 1,742 pages. D. Appleton-Century Company, New York, 1936.

The final part of the book is on radium treatment. Code discusses radium treatment of malignant disease and Donaldson discusses radiotherapy in diseases of women. Code goes deeply into the subject of the principles involved and the action of radium. He describes the biologic effect of this agent and what may be accomplished in various malignancies, with statistics from various surgical clinics of Great Britain.

Donaldson gives an excellent discussion of his subject. He compares the various technics used, the Stockholm plan, the Munich method, the Memorial Hospital method, the Paris technic, in treating carcinoma of the cervix. He states, "When radiotherapy is combined with x-ray treatment the final results are superior to either of these methods of radiation used alone." Fairchild concludes this part with a paper on the High Voltage x-rays in gynecologic malignancy.

This volume is superb in the scope with which the subjects are treated and if the succeeding volumes are of the same nature this system will rank equally with any of the present-day systems of surgery of any other country. For the practicing surgeon this presentation of the English thought and mode should be of inestimable value.

PHILIP F. WILLIAMS.

The *Collected Writings*¹⁰ of Alfred E. Hess appear in two large volumes. Each of them is of more than 700 pages. In spite of this it was necessary to publish 43 articles by title only. This collection was published not merely as a memorial to Hess, but to preserve the continuity and the development of the many subjects in which Hess took such an intimate and prominent part and to which he contributed so freely. There is hardly a discipline in medicine to which he did not make valuable contributions. In addition to the ones with which his name is most prominently connected, may be mentioned his discovery of thromboplastin, a tissue extract for the control of bleeding; his pioneer observation that the vulvovaginitis of children resists treatment because of the coincident infection of the portio vaginalis. Hess was the father of the preventorium in this and other countries to protect children exposed to tuberculosis from further contamination. His main contributions were in scurvy and rickets. He recognized that latent scurvy was of more frequent occurrence than the overt form. He was the first one to understand that the changes in scurvy were due to changes in capillary permeability rather than changes in the blood. His studies on the lability and ready oxidation of vitamin C completely changed the methods of canning vegetables. His studies on rickets are classical. He again brought cod liver oil into prominence, found out the effects of ultraviolet light and discovered that vitamin D can be produced in foodstuffs through irradiation with ultraviolet light.

Altogether this collection with its charming and heartfelt introductory biography from the pen of his lifelong friend, Abraham Flexner, should be generally recommended to the profession.

R. T. FRANK.

This beautiful *tribute to Dr. Henry Asbury Christian*¹¹ from his admiring and grateful associates and former house officers is dedicated to him on the occasion of his sixtieth birthday. Dr. Vaughn has written an appropriate dedicatory foreword, and Dr. Christian's magnificent service to medicine and especially to the Peter Bent Brigham Hospital is recounted in an introduction.

¹⁰Collected Writings. By Alfred E. Hess. In Two Volumes. Volume I, 719 pages; Volume II, 734 pages. Charles C. Thomas, Springfield, Ill., 1936.

¹¹Medical Papers; dedicated to Henry Asbury Christian, physician and teacher, from his present and past associates and house officers at the Peter Bent Brigham Hospital, Boston, Mass. In honor of his sixtieth birthday, Feb. 17, 1936.

The text of one thousand pages comprises one hundred and one contributions on internal medicine. Truly as one reads through this wealth of material presented by his former pupils one may well agree that Dr. Christian's outstanding contribution to medicine has been as he himself has expressed it, "the training of men."

PHILIP F. WILLIAMS.

This is an *appreciation of J. Arthur Harris*¹² edited by the members of the Department of Botany of the University of Minnesota. They discuss Harris as a man, Harris the botanist and Harris the biometrician. A small number of the author's contributions to these two disciplines are given. Among these are four which interest the gynecologist and obstetrician. One of these articles deals with the length and weight of the newborn of various nationalities. It is based on 44,000 records of Sloane Hospital for Women in which only uniparous births of the white race and married women are considered. Differences in length to nationalities (7 were considered) is exceedingly small, in the male 1.01 cm., in females 0.60. The Irish were longest, the Italians shortest, the Irish heaviest, the Russians lightest. Another investigation deals with the relationship between the number of pregnancies and the number of births. This is based on 11,000 cases of which 4,596 were foreign born and 6,415 American-born mothers, the fathers always being of the same nationality. Practically no relationship between the incidence and the number of children brought to term could be found.

R. T. FRANK.

Abellan has written a small monograph on *Subcutaneous Symphyseotomy*,¹³ covering its indications, contraindications, etc. The maternal mortality was 3.2 per cent, the fetal 18.06 per cent.

R. T. FRANK.

¹²J. Arthur Harris. Botanist and Biometrician. Edited by C. Otto Rosendahl, Ross Alken Gortner and George O. Burr. 209 pages. The University of Minnesota Press, Minneapolis, 1936.

¹³La Sinfisiotomia En España. Por Dr. Angel Guerrero Abellan, Barcelona, 1936.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF MARCH 10, 1936

The following papers were presented:

Incontinence of Urine in the Female. Roentgenograms Illustrating Some Functional Observations of the Injured Urethra. Dr. William T. Kennedy. (To be published in a later issue.)

A Consideration of Some of the Aspects of Sterility. Dr. Gerard L. Moench. (For original article, see page 406.)

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF MARCH 5, 1936

The following papers and case reports were presented:

A Statistical Survey of Eclampsia. Dr. R. A. Kimbrough, Jr., and Dr. R. M. Shirey. (For original article, see page 415.)

Palpation of the Fetal Heartbeat Through the Maternal Abdominal Wall. Dr. Robert J. Griffin. (For original article, see page 515.)

Bicornate Uterus With Ovarian, Omental and Pelvic Endometriosis. Dr. Frank J. Frosch. (For original article, see page 490.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF FEBRUARY 21, 1936

The following papers were presented:

The Significance of Fetal Heart Tones in Ablatio Placentae. Dr. Garwood C. Richardson. (For original article, see page 429.)

Benign and Malignant Polyps of the Cervix Uteri. Dr. Clyde J. Geiger. (For original article, see page 465.)

Spontaneously Occurring Painless Labor in Absence of Neurologic Disease. Dr. Marshall Field.

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

MATERNAL WELFARE WORK IN OHIO

A. J. SKEEL, M.D., CLEVELAND, OHIO

THE work in Ohio under the auspices of the Hospital Obstetric Society is essentially an extension of the "Cleveland plan" to cover the entire state. Under the Cleveland plan or group system, a number of hospitals unite to study their obstetric methods and results. We have organized the state into six districts, in each one of which the hospitals act as a group or unit for the purposes of this study. This group study is the pivotal point in the Cleveland plan. Valuable statistics naturally are accumulated as the result of these clinical conferences, but visiting obstetricians from other states, who attend our meetings and then go home to develop a simpler and easier plan for gathering and analyzing sets of figures on maternal and fetal mortalities and morbidities, have missed the vitalizing factor in our organization. Our "group" meeting is an "experience meeting," and its value is due to the interchange of experiences in pathologic cases. The ensuing discussions are essentially "dry clinics" conducted by these leaders for each other's benefit.

Visitors sometimes say, "There is too much professional jealousy in our community for such a plan to succeed." Human nature is the same in Cleveland as it is in Buffalo, Philadelphia, or San Francisco. If the conference is carried on with a sympathetic understanding of the "other fellow's" troubles, suspicion and jealousy are soon replaced by good will and the desire to help.

HOW TO ORGANIZE A HOSPITAL GROUP

The plan can be carried out successfully in any community having several hospitals within easy driving distance. Large cities, such as New York, Philadelphia, or Chicago, can establish several groups. The organization is one of hospitals, not one of individuals.

Call a meeting of the obstetric staffs of several hospitals and select a chairman and secretary. The chairman should be chosen for his standing and reputation as an obstetrician, and for freedom from commercialism and petty jealousy. The secretary must be willing to carry out the tedious details which will devolve upon him. His devotion to the work can make the organization a success. If he does not function, the whole effort will fail.

Meetings are held every two or three months, depending upon how many cases are to be studied. We have found that ten to fifteen cases can be advantageously considered at one meeting, since about one-half of the puerperal deaths occur before viability, and they receive less detailed attention.

Arrange with the local health office to furnish periodically to the group secretary a copy of the certificates of all puerperal deaths occurring in the locality. Have the secretary forward to each hospital the names and dates of the patients upon whom it is to report, as shown by the death certificates. Each hospital should

then have prepared from the chart, and by personal interview with the doctor, if needed, a detailed report of each case. This report is identified by patient's initials, hospital, date, and case number, so that the secretary can check it against the death certificate. All of these reports should be in the hands of the secretary before the meeting is called to order.

The case report should contain all information necessary for a judgment as to (A) diagnosis, (B) evaluation of care both before and after admission, (C) classification according to our plan.

THE GROUP MEETING OR CONFERENCE

After the call to order, reading of the minutes, correspondence, etc., comes the study of the case reports. Upon the ability to elicit discussion and suggestions for better care will depend the success of the group.

The secretary reads aloud the report of the case, without mentioning the name of the patient, the hospital, or the doctor. These should not be identified until after the discussion. Personalities and institutional relations are thus eliminated. The hospital and the doctor may then be named in order to give opportunity for rebuttal of criticism. The doctor often wants to defend the management of the case. Frequently some point, not sufficiently brought out in the history, influenced his handling of the patient. The case is now ready to classify for statistical studies. The classification is adopted after discussion by the group, sitting in judgment, as a jury on the case. Cases before and after viability should be carefully separated, since fatal abortions, ectopic pregnancies, etc., have no bearing on the efficiency of the obstetric department of the hospital. Infections should be carefully differentiated as to whether or not they were acquired in the hospital or before admission. The cause of death as thus established often corrects obvious errors on the death certificate.

The form for classification is one which our experience has shown is well adapted to help in scientific studies, and in attempting to evaluate hospital arrangements and clinical methods for management of patients. We will present this with instructions for its use later. As time goes by, it becomes the duty of the secretary to compile the information thus acquired into statistics which aid in the selection of efficient standards, and point out methods which are deficient. Our conferences broaden the clinical knowledge of the attending obstetricians. They help to break down the isolation of individual hospitals, and to promote friendly relations among the obstetricians of the community. They elevate the obstetric standards of the participating institutions. There is a natural tendency for each to adopt methods which have proved valuable elsewhere. They give opportunity for combined action against harmful practices.

Our State Organization is far from being a completed project. We have at present absorbed only the larger institutions (those with twenty-four or more obstetric beds). About 95 per cent of these are active members. A far more difficult task now confronts us, viz., that of securing the cooperation of the smaller hospitals, and of preparing standards which are useful and practicable for their limited facilities. One of our committees is working on this problem and expects to visit every small hospital in the state during the coming year. Details of what has been accomplished and some of our statistical findings will be presented in a later statement.

THE NORTH DAKOTA COMMITTEE ON MATERNAL WELFARE

JOHN H. MOORE, M.D., GRAND FORKS, N. DAK.

The North Dakota Committee on Maternal Welfare was organized in November, 1935, as one of the regular committees of the North Dakota State Medical Association. Its present membership is made up of *John H. Moore*, Grand Forks, N. D., chairman, *E. M. Ransom*, Minot, N. Dak., *Paul W. Freise*, Bismarek, N. Dak., *J. F. Hanna*, Fargo, N. Dak., and *John D. Graham*, Devils Lake, N. Dak.

Early in its work, the Committee decided to sponsor as many obstetric meetings before the component District Medical Societies as possible. This plan met with the splendid cooperation of the officers of the various societies contacted. It has been more a question of finding time to put on all the progress requested than of creating a demand for them. The Societies at Fargo, Jamestown and Grand Forks have been visited to date, and Devils Lake and Bismarek are to have committee-sponsored programs in April.

To further the program of professional education in obstetrics, it was decided to ask each District Medical Society in the State to appoint a subcommittee on maternal welfare, to consist of three physicians, one of whom was to be a rural practitioner.

Preliminary arrangements are now under way to hold at least one two-day obstetric seminar during the year, to be conducted by a prominent obstetrician from without the state. The chief subjects to be discussed at this seminar are: (1) Prenatal care, (2) the prevention of infection, (3) the prevention and control of the toxemias of pregnancy, (4) the prevention and management of abortions, (5) breast feeding.

The Committee has had splendid cooperation from *Maysil M. Williams*, State Health Officer for North Dakota. Through the State Department of Health, sterile obstetric packages for home deliveries are to be made available to private physicians requesting them. With the endorsement of the Committee and under the direction of Dr. Williams, a Maternity Nursing Service is to be instituted in one county in the state for a period of one year.

The Committee has stressed the importance of well-equipped, separate obstetric departments in hospitals admitting maternity patients, adequate nursery facilities, and the importance of isolation of any infected patients. The State Board of Administration, which licenses all hospitals or maternity homes in the State, will be asked to check all so-called maternity homes, especially in regard to equipment and whether or not registered nurses are in charge.

To date, eight radio talks on maternal welfare have been broadcast under the sponsorship of the committee. Because of the response to this feature of lay education, it was decided to prepare and broadcast a series of four talks on infant welfare, and this material is now being prepared. Home-makers Clubs in North Dakota are very active and the committee was approached as to the possibility of providing a course of study, dealing with maternal and infant welfare, for club meetings.

The program of the committee is just getting under way in North Dakota. It represents the attempt of organized medicine to meet the demands of the profession and laity for a better understanding of the problems involved in maternal welfare. We believe that one of the chief functions of the committee should be

the placing of emphasis on the personal relationship between patient and physician. Our program is the antithesis of state medicine or of socialized medicine in any form. Only through the personal cooperation of the physicians of the state and the education of the patients to seek the highest type of obstetric service available to them can this program or any other program of maternal welfare succeed. The response to our efforts to date has made us optimistic for the future.

OBSTETRICS IN INDUSTRIAL MEDICINE

GOODE R. CHEATHAM, M.D., ENDICOTT, N. Y.

(From the Obstetrical Departments of the Endicott-Johnson Medical Service and Ideal Hospital)

THE following is a brief summary of the first 1,000 consecutive deliveries done at Ideal Hospital by the Obstetrical Department of the Endicott-Johnson Medical Service. Its chief interest lies in the fact that these cases were part of the work of a form of industrial medicine. Obstetrics is not usually considered a part of industrial medicine, hence it was thought that at a time when every form of state, group, and social medicine imaginable is being urged upon the profession, the results of this form of industrial medicine would be of general interest.

The series consists of all deliveries done from Feb. 16, 1932, to Aug. 11, 1935 (abortions excluded).

991 mothers delivered 1,000 babies (9 sets of twins)

840 deliveries were nonoperative

160 deliveries were operative

Operative deliveries were:

A. Forceps	125
High	1
Mid	21
Low	103
B. Version	18
C. Cesarean	18

The results were:

Maternal:

Mortality (uncorrected)	1
Mortality (corrected)	0
Morbidity (uncorrected)	79
Morbidity (corrected)	41

Morbidity standard was any temperature of 100.4° F. or over for any two days exclusive of the first twenty-four hours.

Fetal:

Stillbirths	25
Stillbirths without fetal heart on admission	13
Stillbirths with fetal heart on admission	12
Neonatal	
Babies of any age dying before discharge	36
Babies under 1,500 gm., or 28 weeks of age	19
Babies over 1,500 gm., or 28 weeks of age	17
Total corrected fetal mortality	29

Obstetric complications were not unusual except that Bandl's ring was noted far more frequently than is generally reported. It occurred six times. Whether these were all a true Bandl's ring or were the so-called persistent contraction ring or not is debatable, for none was left undelivered once the diagnosis of a ring was made. The frequency of these rings aroused our interest, and a review of the cases showed that they were not confined to the cases of prolonged labor, and that morphine in the first stage did not prevent them. Pituitrin was not a factor, for it was not used in any case until the second stage had been completed.

Nonobstetric complications were not properly indexed but the following were noted: diabetes mellitus, 2; pulmonary tuberculosis, 1; severe secondary anemia, 3; salpingitis, ?; cardiac failure, 4; hyperthyroidism, 2; mastoiditis, 2; pyelitis, ?; measles, 1 scarlet fever, 1.

The one maternal death was a patient who was seen at the office prior to delivery, suffering from acute catarrhal otitis media. She was referred to the otologist who did a paracentesis. A few days later she was admitted to the hospital in active labor, delivered spontaneously without vaginal examination and without lacerations. She was placed in isolation immediately because of her discharging ear. The otologist saw her and took charge of the ear condition. Nine days postpartum she developed an acute mastoiditis, was operated upon, became worse, developed a brain abscess, and was reoperated upon. She became progressively worse and finally died several weeks after delivery. The baby was discharged from the hospital as a well baby. This case was not considered as a death from puerperal causes.

The series is too small for the individual procedures, with their results, to have any significance.

A study of the results shows a high uncorrected neonatal death rate of 36 per 1,000 total deliveries. This is the big obstetric problem here. Many of the patients work during pregnancy and many are admitted to the hospital in the latter months of pregnancy with labor far advanced. Many of these babies are previsible, yet not stillborn, and many more that are theoretically viable die of prematurity despite incubators, oxygen therapy units, etc. What effect, if any, industry has on premature labor and abortions cannot be accurately determined, but I am fully convinced that in any highly industrialized community where large numbers of women are employed, the percentage of abortions and premature labors, with the attendant loss of many babies, will always be large.

A few very definite obstetric principles were followed in this series of cases, which were all done in a small general hospital. They were: conservative treatment of eclampsia, cesarean section for central placenta previa, frequent and sufficiently large blood transfusions, and a policy of noninterference with labor, unless there were definite indications. This last policy was not rigidly adhered to in the case of low forceps. We do not believe in routine low forceps, neither do we believe low forceps to be as harmful to the baby as prolonged labor. The total operative incident excluding low forceps was 5.7 per cent.

COMMENT

This series of cases constitutes over one-half of the total deliveries in this area for the time covered by the series, and accounts for the exceptionally high percentage of hospital deliveries in this area (84.7 per cent for 1935), yet the five-year average maternal mortality here is 5.38 per 1,000 births, and has not been lowered appreciably by this series.

A properly regulated general hospital can be made safe for maternity cases and is to be preferred to the home.

Items

American Board of Obstetrics and Gynecology

The next written examinations and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology will be held in the various cities in the United States and Canada on Saturday, November 7, 1936, and on Saturday, March 6, 1937.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for these examinations must be filed in the Secretary's office sixty days prior to the scheduled date of examination.

Central Association of Obstetricians and Gynecologists

The Eighth Annual Meeting of The Central Association of Obstetricians and Gynecologists will be held at the Hotel Statler in Detroit on October 15, 16, and 17. The guest speaker will be Dr. Emil Novak of Baltimore. The profession is cordially invited.

Dr. Ralph A. Reis, Secretary
104 South Michigan Avenue
Chicago, Ill.

American College of Surgeons

At the next annual meeting of the American College of Surgeons to be held in Philadelphia, during the week beginning Monday, October 19, the following program of especial interest to obstetricians will be presented on the opening day at two o'clock at the Bellevue Stratford Hotel.

Presiding, George W. Kosmak, M.D., Editor, AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY.

"The Adequate Care of the Obstetric Patient in the General Hospital."

(a) "From the Standpoint of the Specialized Practice of Obstetrics." Charles C. Norris, M.D., Philadelphia, Professor of Obstetrics and Gynecology and Director of Department, University of Pennsylvania.

(b) "From the Standpoint of the General Practice of Medicine." Walter Brand, M.D., Toledo, Director of Obstetrics, Women's and Children's Hospital.

(c) "From the Standpoint of Analgesia and Anesthesia." Edward L. Cornell, B.Sc., M.D., Chicago, Assistant Professor of Obstetrics, Northwestern University Medical School, Member of Staff, Chicago Lying-In Hospital.

(d) "From the Standpoint of Nursing Care." Clara M. Konrad, R.N., Jersey City, N. J., Assistant Superintendent and Directress of Nurses, Margaret Hague Maternity Hospital.

(e) "From the Standpoint of the Administration." C. S. Woods, M.D., Cleveland, Superintendent, St. Luke's Hospital.

"The Control of Morbidities and Mortalities." John R. Fraser, M.D., Montreal, Professor of Obstetrics and Gynecology, McGill University Faculty of Medicine.

"Graduate Training for Obstetrics." George W. Kosmak, M.D., New York, N. Y.

"The Work of the Committee on Maternal Welfare." Fred L. Adair, M.D., Chicago, Professor of Obstetrics and Gynecology, University of Chicago.

Holland Gynaecological Society

We have been informed that the Holland Gynaecological Society at Amsterdam has decided to organize an *International Congress for Obstetrics and Gynaecology at Amsterdam* in connection with its fiftieth anniversary in 1938.

The last International Congress for Obstetrics and Gynaecology was held in Berlin in 1912. Further particulars regarding the project will be published in this JOURNAL.

The Secretary of the Committee organizing the Congress at Amsterdam is Dr. F. C. van Tongeren, University Clinics for Obstetrics and Gynaecology, Wilhelmina-Gasthuis, Amsterdam W.

The Second All India Obstetric and Gynaecological Congress

The Second All India Obstetric and Gynaecological Congress will be held in Bombay about December 25, 1937. The following are the subjects selected for the principal discussions: (a) Toxemia in Pregnancy, and (b) Cancer of Cervix. The exact time and program will be announced in due course of time.

Books Received

THE SINGLE, THE ENGAGED AND THE MARRIED. A treatise on the mutual adjustment for the attainment of happiness in marriage. By Maurice Chideekel, M.D. 268 pages. Eugenie Publishing Company, Inc., 1936.

THE BABY AND GROWING CHILD. Feeding and Health Care. By Louis Fischer, M.D., consulting physician of the Willard Parker Hospital, New York City, etc. Illustrated. 260 pages. Funk & Wagnalls Company, New York City, 1936.

THE TOXAEMIAS OF PREGNANCY. By Dame Louise McIlroy, consulting obstetrician and gynaecologic surgeon, Royal Free Hospital, etc. 355 pages. William Wood & Company, Baltimore, 1936.

UROLOGY IN WOMEN. By E. Catherine Lewis, M.S.(Lond.), F.R.C.S.(Eng.), surgeon to Royal Free Hospital, etc. Second edition. Illustrated. 100 pages. William Wood & Company, Baltimore, 1936.

FOOD, FITNESS AND FIGURE. By Jacob Buckstein, M.D., consulting physician in diseases of stomach and intestines, United States Veterans' Bureau, etc. 252 pages. Emerson Books, Inc., New York City, 1936.

ARBEITSPHYSIOLOGIE DER SCHWANGERSCHAFT. Von Dr. Med. Fritz Stachler, Oberarzt an der Universitätsfrauenklinik in Frankfurt a.M. Mit 16 Kurven und 17 Abbildungen im Text. 103 Seiten. Verlag von S. Karger, Berlin, 1936.

VITAMINE DER MILCH. Dr. Med. Walter Neuweiler, Universitäts-Frauenklinik, Bern. 140 Seiten. Verlag von Hans Huber, Berlin.

BLUTUNG UND FLUOR. Von Professor Dr. Hans Runge, Direktor der Universitätsfrauenklinik, Heidelberg. Zweite, erweiterte Auflage, mit 18 Abbildungen auf 117 Seiten. Verlag von Theodor Steinkopf. Dresden, 1936.

FIRST ALL- INDIA OBSTETRIC AND GYNAECOLOGICAL CONGRESS, MADRAS. 2nd to 4th, January, 1936. Proceedings.

LES PROBLÈMES D'ONCOLOGIE. Tome VII. Édition Médicale d'État D'Ukraine, 1935. (In Russian.)

THE MARRIED WOMAN. By Gladys H. Groves and Robert A. Ross, M.D. 278 pages. Publishers: Greenberg, Inc., New York, 1936.

ENDOCRINOLOGY IN MODERN PRACTICE. By William Wolf, M.D. With 252 illustrations and 1018 pages. W. B. Saunders Co., Philadelphia, 1936.

WILLIAMS OBSTETRICS. By Henricus J. Stander, Professor of Obstetrics and Gynecology, Cornell University Medical College, etc. Seventh edition, a revision and enlargement of the text originally written by J. Whitridge Williams. With 278 illustrations and 1269 pages. D. Appleton-Century Company, New York, 1936.

American Journal of Obstetrics and Gynecology

VOL. 32

OCTOBER, 1936

No. 4

American Gynecological Society *Sixty-First Annual Meeting*

PRESIDENT'S ADDRESS

B. P. WATSON, M.D., NEW YORK, N. Y.

HUMAN feeling may be expressed in many ways: by the artist in form and in color, by the musician in composition and in interpretation, and by the writer in words so phrased as to bring to us his inner meaning.

My only medium is words, and I regret that I have not that facility in their use which would serve to convey to you all of the emotions which have stirred in me since you honored me by electing me your President.

There was first and uppermost the feeling of pride and joy that this honor should have come to me at your hands; but there has been also a constant undercurrent of doubt and dismay born of a realization of the lack in me of those qualities and attainments which have distinguished my predecessors in this Office. That you, in spite of these deficiencies, should still have deemed me worthy, places me forever in your debt for thus conferring upon me the greatest honor of my professional career.

In the year that has passed since our last meeting, death has taken a heavy toll; eight, Fellows, three of them former Presidents, have passed away. It is fitting that we pause for a brief space and recall them to memory.

NOTE.—This issue is, and a portion of the November number of the JOURNAL will be, devoted to the transactions of the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936. The papers are presented approximately in the order of their reading, together with the abstracted discussions. All of the contributions to the program are included with the exception of a paper by Dr. F. C. Irving, entitled "The Histologic Pathology of Placenta Accreta," which will appear in Surgery, Gynecology, and Obstetrics.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

William Blair Bell was elected to Honorary Fellowship in 1922 as a mark of appreciation, from his Colleagues here, of the work carried on by him in England. Honored in his own country as the first President of the British College of Obstetricians and Gynecologists, his death is a loss to the world at large.

Dougal Bissell was a very frequent contributor to our Transactions and will always be remembered for his investigations on the structures of the pelvic floor, and for the operative procedures which he devised and carried out for the repair of obstetric injuries.

Sir Kedarnath Das, elected an Honorary Fellow in 1923, was our guest in 1922, when he spoke to us on obstetric practice in India. He contributed much to scientific obstetrics and did an enormous service to India in raising the standards of teaching and practice in that vast country.

Francis Henry Davenport became a Fellow in 1889, was elected to the Honorary Fellowship in 1914, and died in the spring of this year at the age of eighty-five. He was for many years a teacher in the Harvard Medical School and practiced gynecology in Boston until 1914 when he retired from active work.

George Gellhorn had been a Fellow of the Society for thirty-two years and was President in 1932. He was a tireless worker, a man of original ideas, who was never afraid to put them to a practical test, a master of the English language, a philosophic thinker, and, at the same time, essentially a man of action. We all mourn his death and miss him.

In Barton Cooke Hirst, President in 1924, we have lost the doyen of our specialty in this country. He was a genial gentleman of the old school and was also a most up-to-date obstetrician and gynecologist, who has left his mark indelibly written on our records. We mourn for him as a scientist and as a dear friend.

Charles P. Noble was elected to the Society in 1891 and was Treasurer for some years. He was a prolific writer on obstetric and gynecologic subjects, and even after his retirement from active work he continued to interest himself in biologic problems.

C. Jeff Miller will always live in our memories as one who combined in a remarkable degree the attributes of the perfect gentleman, the genial companion, the cultured, widely read man, the practical investigator and teacher, and the wise counselor. His passing takes from us one whom we could ill spare. He occupied the President's Chair in 1929.

A wide latitude is allowed your President in a choice of a topic for his Address. During the ten years which have elapsed since I left my native Scotland to settle here and to become one of you (and for the heartiness of your welcome and for your unstinted kindness, I can never adequately express my appreciation), I have been increasingly interested in the exchange of ideas which has taken place between the two countries and, especially, in the influence that the Medical School of my Alma

Mater, the University of Edinburgh, had on the early development of medical education and practice here. I propose to recall to your memory some of the incidents and individuals in this connection.

In the days of the young American Colonies and at the time of the Declaration of Independence, the Medical School of Edinburgh was among the most renowned and the most progressive in Britain and in Europe. It was strong both on the surgical and on the medical side and was especially strong in anatomy. Its surgical and anatomical school began when, in the year 1505, the Town Council of Edinburgh granted a Charter to the Barber-Surgeons and recognized them as a distinct Craft. The present Royal College of Surgeons is the direct descendant of that Craft.

At the time of their incorporation, the Barber-Surgeons petitioned for and were granted the privilege of receiving from the City the body of one condemned man each year for dissection. This showed extraordinary enlightenment on the part of the Craft and of the City Fathers, for remember that at that time the Fathers of Anatomy, Vesalius and Fallopius, were not yet born, and that the Divines had not yet met at Salamanca "to determine if it were consistent with conscience to dissect the human body for the purposes of science." The Edinburgh Town Council not only granted the privilege, but they enjoined that the dissection be performed in public. Thereafter, each year the Craft appointed several of its members to carry out this dissection, each member taking up a different part of the body.

Very soon it was found that one body a year was not sufficient, and in the early Seventeenth Century the Barber-Surgeons again petitioned the Town Council and from it obtained permission to acquire "the bodies of fundlings who dye betwixt the tyme that they are weaned and their being put to schools or trades; also the dead bodies of such as are stifled in the birth, which are exposed and have none to owne them; as also the dead bodies of such as are felo de se, and have none to owne them; likeways the bodies of such as are put to death by sentence of the magistrat, and have none to owne them." The Council granted all this on condition that the surgeons before the year 1697 should have ready a properly equipped anatomie theater in which at least one public dissection each year be carried out. There is a full account in the records of the College of such a dissection performed in the year 1703. Eight members of the Craft took part in it, and the scene, as Miles says, must have been "not unlike that depicted by Rembrandt in his *Lesson on Anatomy*."

Meantime the schools of anatomy in Europe were flourishing and notable discoveries were being made so that Scottish youths were attracted to the Continent for anatomie study. For their better instruction the Town Council, therefore, determined to appoint one man as Professor of Anatomy at a salary of £15 a year and to put on him the

responsibility of all teaching. Their reasons for this step were what are generally regarded (outside Scotland) as peculiarly Scotch, viz. "as an encouragement to young men to stay at home instead of travelling to foreign universities which is attended by expenses and other perils to youth."

The man appointed was Robert Eliot; the date of his appointment was 1705. He was the first Professor of Anatomy in Britain. This was the beginning of the Edinburgh School of Anatomy and was the foundation of the reputation which the Edinburgh Medical School held throughout the intervening years for anatomic teaching and research.

Eliot was succeeded by McGill, and then in 1720 Alexander Munro was appointed. He was succeeded by his son, Alexander Munro, secundus, and he, in turn, by his son, Alexander Munro, tertius, so that the professorship of anatomy remained in the hands of the Munro family for one hundred and twenty-six years. During these years students flocked to Edinburgh from all parts of the world. At one time there were as many as 800 students, many of them from the American Colonies, resident in the city for the study of anatomy alone.

The Colonists were also attracted to Edinburgh by the caliber of those who were teaching the practice of medicine. In the year 1726 a number of professors were appointed to the Edinburgh faculty. All of them had studied in Leyden under Boerhaave, the acknowledged Father of Clinical Medicine. They brought to Edinburgh his methods and tried to develop there a school like that of their master. Andrew St. Clair and John Rutherford were the pioneers, along with Robert Whytt at a later date.

In 1766 William Cullen was appointed Professor of Medicine and became the "Boerhaave" of Scotland. These were the men who attracted to Edinburgh young American colonists, who after obtaining their degrees returned to practice in their own land.

Benjamin Franklin was a great personal friend of Cullen and recommended many promising young men to him, among others William Shippen and Robert Morgan. Here is a letter from Franklin to Cullen written in 1760:

I thank you for the civilities you were so good as to show my friend, Mr. Shippen, whom I took the liberty of recommending to your notice the last year. Give me leave to recommend one friend more to your advice and countenance. The bearer, Mr. Morgan, who purposes to reside some time in Edinburgh for the completion of his studies in physics, is a young gentleman of Philadelphia, whom I have long known and greatly esteem; and as I interest myself in what relates to him, I cannot but wish him the advantage of your conversation and instructions. I wish it also for the sake of my country, where he is to reside, and where I am persuaded he will be not a little useful.

Shippen graduated in Edinburgh in 1761, Morgan in 1762, and Benjamin Rush in 1768. Those three men, together with Adam Kuhn, also

an Edinburgh graduate, were the founders in Philadelphia of the first medical school in this country. The year was 1763.

While resident in Scotland, Rush became very friendly with a Presbyterian minister in Ayrshire, a descendant of John Knox, named Witherspoon. Witherspoon was invited to become the President of Princeton but refused. A second invitation was extended him and on the urgent pleading of Rush he accepted. Later both Witherspoon and Rush were signatories to the Declaration of Independence.

Samuel Bard was also a favorite pupil of Cullen. He graduated with the degree of M.D. in Edinburgh in 1765, and in 1769 became the first Professor of the Theory and Practice of Medicine in Kings College (now Columbia University), New York. To him New York owes the foundation of the City Hospital. Curiously enough, although Professor of Medicine, he wrote the first treatise on obstetrics in his country. David Hosack graduated in Edinburgh in 1794 and Latham Mitchell in 1784. "These three men (Bard, Mitchell, and Hosack) laid the foundation of the medical institutions of New York." (Osler.)

I should like to be able to say that Thomas Addis Emmet was a graduate of Edinburgh but I cannot do more than claim that his grandfather was one, of the year 1784. I should, likewise, like to claim Ephraim McDowell, the Father of Ovariectomy, but must be content with the fact that he did study anatomy and surgery under John Bell in Edinburgh during the years 1793 and 1794.

All of these great Americans retained a love for Scotland and Edinburgh as is shown by the letters they wrote to their former teachers, some of which I should like to quote to you but time forbids.

This fine exchange of courtesies was likely to be broken a century later when in 1870 Dr. Jacob Bigelow of Boston and Sir James Young Simpson of Edinburgh engaged in a wordy warfare over the priority of the discovery of general anesthesia and over the relative merits of ether and chloroform.

I suppose that most of us are to some extent hero worshipers, and I confess that Simpson is one of my heroes. This, in spite of the fact that in the writing of history in these latter days hero worship is no longer the vogue. The modern attitude is rather one of cold analysis with often an exaggerated emphasis on the faults and failings of the individual under discussion, bringing him down to our common level and ascribing to the times in which he lived and the attending circumstances the major credit for what he had achieved. Thus, Singer writing of Vesalius, the Father of Anatomy, says: "... he is in a sense, a lucky man in the position he holds in the scientific world. His great work was not the result of a long lifetime of experience . . . ; it was not wrought in the fierce heat of an intellectual furnace as was that of Pasteur or of Claude Bernard; it was not a task of subtle reasoning and skilled experimenting as was that of Harvey and of Hales. Vesalius was a very char-

acteristic product of his age. The womb of Time was in labor and it brought him forth. His intellectual father was the Galenic science that had gone before him. His mother was that fair creature the New Art, then in the very bloom of her youth. Until these two had come together there could be no Vesalius. When these two had come together there had to be a Vesalius."

Most epoch-making discoveries have been very simple in nature and almost self-obvious when expounded. The real kernel of many of them had been known years before the man or men arose who had the vision to perceive their importance and the energy and ability to work them out and to put them to practical use. These latter, rightly or wrongly, get the major credit for them.

In the history of the discovery of the principles of general anesthesia, the different anesthetic agents and their uses in surgery and obstetrics, these statements are amply illustrated. Around no other series of discoveries has such a warfare raged as that which followed the discovery of general anesthesia.

After Morton's successful demonstration of the anesthetic properties of ether in Boston in 1846, he was hailed as the hero and the pioneer. Horace Wells, who had induced anesthesia with nitrous oxide in 1844, and whose pupil Morton was, was for the time being forgotten, as was also Charles T. Jackson, Professor of Physics at Harvard, who had suggested the use of ether to Morton.

And Sir Humphry Davy was scarcely mentioned in spite of the fact that it was he who in the year 1800 had discovered the general anesthetic properties of nitrous oxide and had used it on himself for the relief of pain.

So heated did these discussions become that a Selected Committee of the Senate of the United States was appointed to settle the matter and their findings were published in a large volume of "Official Documents." Concurrently with and following this domestic discussion in the United States there arose the international dispute between Dr. Jacob Bigelow of Boston and Sir James Young Simpson of Edinburgh, Scotland, to which I have referred.

This controversy arose as the result of Bigelow's reading in an Edinburgh newspaper an account of the presentation of the Freedom of the City to Sir James Simpson. The Lord Provost in the course of his short speech of presentation said: "I will not dwell on what you have accomplished in medical science. I will only allude to the discovery—the greatest of all discoveries in modern times—of the application of chloroform in the assuagement of human suffering."

Bigelow upbraided Simpson because in his reply he made no mention of ether and of the discovery of its anesthetic properties by Morton in Boston. They were both accomplished letter writers and stated their

views in no uncertain way, and the whole correspondence makes most lively reading now. There was much misunderstanding on both sides but ultimately they agreed on the pertinent facts.

At the end of a very long letter to Bigelow, dated from Edinburgh, April, 1870, Simpson concludes the correspondence thus:

If we try to put into a summarized form the data which we have been discussing regarding the introduction of anesthesia in America and this country, it appears to me that we might correctly state the whole matter as follows:

1. That on the eleventh of December, 1844, Dr. Wells had, at Hartford, by his own desire and suggestion, one of his upper molar teeth extracted without any pain, in consequence of his having deeply breathed nitrous oxide gas for the purpose, as suggested nearly half-a-century before by Sir Humphry Davy.

2. That after having with others proved, in a limited series of cases, the anesthetic powers of nitrous oxide gas, Dr. Wells proceeded to Boston to lay his discovery before the Medical School and Hospital there, but was unsuccessful in the single attempt which he made, in consequence of the gas-bag being removed too soon, and that he was hooted away by his audience, as if the whole matter were an imposition, and was totally discouraged.

3. That Dr. Wells's former pupil and partner, Dr. Morton of Boston, was present with Dr. Wells when he made his experiments there.

4. That on the thirtieth of September, 1846, Dr. Morton extracted a tooth without any pain, while the patient was breathing sulphuric ether, this fact and discovery of itself making a NEW ERA in anesthetics and in surgery.

5. That within a few weeks the vapour of sulphuric ether was tried in a number of instances of surgical operations in Boston—Dr. Morton being generally the administrator; and ether vapour was established as a successful anesthetic in dentistry and surgery.

6. That in January, and the subsequent spring months, 1847, the application of sulphuric ether as an anesthetic in midwifery was introduced, described in our medical journals, and fully established in Edinburgh, before any case with it was tried in Boston or America.

7. That on the fifteenth of November, 1847, the anesthetic effects of chloroform were discovered in Edinburgh, and that it swiftly superseded in Scotland and elsewhere the use of sulphuric ether, and extended rapidly and greatly the practice of anesthesia in surgery, midwifery, etc.

The letter continues:

I am very sorry to have taken up so much of your time and my time with such a petty discussion as the present. It has extended to too great a length; but I am a sad invalid just now, and quite unable to write with the force and brevity required. With many of our profession in America I have the honour of being personally acquainted, and regard their friendship so very highly that I shall not regret this attempt—my last perhaps—at professional writing as altogether useless on my part, if it tend to fix my name and memory duly in their love and esteem.

Yours very truly,

J. Y. SIMPSON.

The news of Simpson's death reached Boston by cable before his letter arrived and the Gynecological Society of Boston held a Memorial Meeting in honor of their "late beloved associate" who was, they said, "one of nature's noblemen."

Thus, the ultimate result was that Simpson freely acknowledged, as he had always done, that Morton was the first man to produce general anesthesia to the surgical degree by the administration of ether, and Bigelow acknowledged that Simpson was the first man to use ether as an anesthetic in obstetrics, and that he discovered the anesthetic properties of chloroform.

Neither of these contributions of Simpson came to fruition in any haphazard way. Both were the result of deep thought and of hard experimental work. Both were defended against the attacks of all sorts and conditions of people with a dialectic skill and a dogged persistence which mark Simpson as a real man of genius, if genius consists of "an infinite capacity for taking pains."

Let us first try to picture what sort of man he was. Born of poor parents (his father was a baker) in the village of Bathgate in the year 1811, he was the youngest of seven children. His early education was begun in the village school at the age of four in the year of the Battle of Waterloo, and completed at the age of fourteen when he entered the Faculty of Arts of the University of Edinburgh.

As was common with poor Scots' families of these times and later, all of the family resources were called upon and all sorts of economies were effected in order to provide funds to send the promising son to college. And James Simpson gave great promise, for not only was he head of his school at the age of fourteen but had already, in the study of the flora and geology of the countryside, begun to show that power of observation and that faculty for the acquisition of facts which characterized all his later scientific work.

He never completed his Arts course, for after two years he was attracted to medicine. He had attended all the necessary classes and passed his final examination for the medical degree while still in his teens and had to wait for two years before he could be licensed to practice. This time was occupied in attending again the class of midwifery, in acting as assistant to the professor of pathology, in assisting the doctor in his native village, and in travel to London and to the Continent of Europe. The funds for the latter were again provided by his devoted family.

He began his professional career in Edinburgh as a general practitioner but early devoted his attention to midwifery, obtaining an appointment to the Lying-In Hospital and starting a lecture course for students in obstetrics.

Meantime, he had begun to write and to publish papers on pathology which received wide attention, not only in Scotland but also in Europe.

When he was twenty-eight years old, the professorship of midwifery in the University fell vacant and Simpson became a candidate for the Chair. The power of appointment was in the hands of the Town Council of the City and the contest between Simpson and his chief rival, Ken-

neddy of Dublin, was very keen. Simpson put all of his enormous energy into the fight, even going so far as to acquire a wife at short notice, when he learned that his state of bachelorhood was being used as an argument against him. He spent £500, a large sum in those days, on the preparation and distribution of his testimonials, which made a volume of 150 octavo pages. "His aim was to make known his scientific attainments, powers as a teacher, and personal qualifications, which he felt, if duly realized, would outweigh the disadvantages of his youth and comparative inexperience."

After a spirited contest he was elected by a majority of one and with that matter settled immediately directed his prodigious energy and enthusiasm to his chosen subject.

Not content with the narrower field of obstetrics he did pioneer work in the field of diseases of women, and must be regarded as one of the founders of modern gynecology. Had he done nothing at all for anesthesia his name would have lived for his contributions to this subject.

Simpson was an omnivorous reader, not only of medical but also of general and, especially, of antiquarian literature, and (as we shall see presently) was a theologian of no mean order who knew his Bible from beginning to end. A man of fine sensibilities, the suffering of his parturient patients always distressed him. He tried all sorts of drugs and even resorted to experiments in hypnotism in an effort to relieve them. Among all his other interests, this one was ever present in his mind.

When, therefore, news reached Edinburgh from across the Atlantic that Morton in Boston on Oct. 16, 1846, had successfully induced anesthesia by the inhalation of ether and that Liston had subsequently used it in London, Simpson was thrilled and immediately thought of its possibilities in obstetrics.

The problem that faced him was a harder one than that which confronted the surgeon. In those days the surgeon did his work quickly, so that the patient did not require to be long under the influence of the anesthetic.

The problem presented to Simpson was twofold. Could the anesthesia be continued sufficiently long to give appreciable relief? And would the anesthetic interfere with uterine contraction?

He chose for the first trial a case of contracted pelvis, calling for the operation of version. He waited for this case because, from the nature of the operation, any interference with uterine contraction by the anesthetic would be of little moment. On Jan. 19, 1847, the operation was successfully and painlessly performed under ether anesthesia, and Simpson was able to satisfy himself that uterine contraction went on normally. He, therefore, proceeded to employ it in normal cases, an account of which he read before the Edinburgh Obstetrical Society

on Feb. 10, 1847. The practice was soon taken up in Scotland, in England, in Germany, and, a few months later, in America.

Not being altogether satisfied with ether, because of the large quantities required in prolonged cases, and because of the bronchial irritation to which it often gave rise, he had sent to him by different chemists various volatile substances which might be inhaled. With these he experimented on himself and on his friends.

Among these substances was a small quantity of chloroform, which he had procured from Messrs. Duncan and Flockhart. Mr. Waldie, a Scotsman in business as a chemist in Liverpool, had suggested to him that this was probably the anesthetic substance in the chloric ether which Bigelow in Boston and Liston and Jacob Bell in London, had used successfully.

Here is the story of the discovery, as it is graphically told by Professor Miller, a near neighbor of Sir James Simpson in Queen Street, Edinburgh, and quoted by his nephew and successor in the Chair, the late Sir. A. R. Simpson:

Most of these experiments were performed after the long day's toil was over, at late night or early morn, and when the greater part of mankind were soundly anesthetized in the arms of common sleep. Late one evening, it was Nov. 4, 1847, on returning home after a weary day's labor, Dr. Simpson with his two friends and assistants, Drs. Thomas Keith and J. Mathews Duncan, sat down to their somewhat hazardous work in Dr. Simpson's dining room. Having inhaled several substances, but without much effect, it occurred to Dr. Simpson to try a ponderous material, which had been formerly set aside on a lumber table, and which, on account of its great weight, he had hitherto regarded as of no likelihood whatever. That happened to be a small bottle of chloroform. It was searched for, and recovered from beneath a heap of waste paper. And, with each tumbler newly charged, the inhalers resumed their vocation. Immediately an unwonted hilarity seized the party; they became bright-eyed, very happy, and very loquacious, expatiating on the delicious aroma of the new fluid. The conversation was of unusual intelligence, and quite charmed the listeners, some ladies of the family and a naval officer, brother-in-law of Dr. Simpson. But suddenly there was a talk of sounds being heard like those of a cotton mill, louder and louder; a moment more, then all was quiet, and then, a crash. On awakening, Dr. Simpson's first perception was mental: "This is far stronger and better than ether," he said to himself. His second was to note that he was prostrate on the floor, and that among the friends about him there was both confusion and alarm. Hearing a noise, he turned round and saw Dr. Duncan beneath a chair, his jaw dropped, his eyes staring, his head bent half under him; quite unconscious, and snoring in a most determined and alarming manner. More noise still, and much motion. And then his eyes overtook Dr. Keith's feet and legs making valorous efforts to overturn the supper table, or more probably to annihilate everything that was on it; I say, more probably, for frequent repetitions of inhalation have confirmed, in the case of my esteemed friend, a character for maniacal and unrestrainable destructiveness, always under chloroform, in the transition stage.

By and by, Dr. Simpson having regained his seat, Dr. Duncan having finished his uncomfortable and unrefreshing slumber, and Dr. Keith having come to an arrangement with the table and its contents, the sederunt was resumed. Each expressed himself delighted with the new agent, and its inhalation was repeated many times that night, one of the ladies gallantly taking her place and turn at the table, until

the supply of chloroform was fairly exhausted. It is of interest to note that Keith was elected to the honorary fellowship of this society in the year of its foundation and Mathews Duncan two years later.

There can now be no question but that to Simpson belongs the sole credit of being the first to suggest and to use general inhalation anesthesia in labor, and that he was the first to demonstrate the anesthetic property of chloroform. While time has not confirmed Simpson's assertion that chloroform was a better and safer anesthetic than ether, some of us still regard it as having a very definite place in obstetrics.

But with these discoveries, Simpson's task had only just begun, for immediately there arose a clamor from the medical profession and from the Church against the use of anesthetics in labor. It was fortunate that Simpson was a man of such strong convictions, such iron will, and so skilled in debate as to beat down that opposition.

One of his most bitter opponents was Professor Meigs of Philadelphia. Which of us today could write as Simpson did to Meigs in 1848? His letter begins as follows:

Edinburgh, August, 1848

My dear Sir:

A few days ago, I saw your excellent epistle to me on the use of anesthesia in midwifery, extracted, in an abridged form, from the Philadelphia Medical Examiner of March last, into the London Medical Gazette and Lancet. It reminded me, that amid other avocations and work, I had hitherto indolently omitted to answer the objections contained in your able and kind letter. And I feel that I am the more to blame for this neglect, on one account, namely, that as in your own country, so also in ours, there are few or no living obstetricians, whose opinions and names carry, and deservedly carry, more weight with them than yours. Be so good, then, as to bear with me now for a few minutes, while I endeavor to state in what respects I am inclined to demur to your arguments against anesthetic midwifery.

On reperusing, as I have just done, your esteemed letter, it appears to me that in it you ground your opposition to the adoption of anesthesia in midwifery upon four or five different arguments, although you do not specialize them. I shall notice each of these arguments separately. You have not placed them in any particular order. I shall begin first with the one which you placed last.

So polite and yet with such veiled sarcasm. He then proceeds to demolish each of Meigs' arguments, the whole letter extending to twenty closely printed pages. Allow me to quote one small section of his reply to Meigs' objection to anesthesia in natural labor, on the ground that the pain of natural labor is a "physiological pain":

You are well aware that the act of parturition has been often familiarly compared, as the late Professor Hamilton expressed it, "to the toils of a journey," and like it divided into stages. "The sufferings of the mothers," says he, "have been in most languages compared to those of travellers." Now let us for a moment continue this natural simile between the function of parturition and the function of progression. You maintain that "labour is the culminating point of the female somatic forces." One of the most illustrious Presidents of your great American Republic, Thomas Jefferson, makes in his memoirs a remark of precisely the same

import regarding walking or progression. He describes the act of walking, but not exactly in the same words, as a kind of "culminating point of the human somatic forces."

"Walking," says the American President, "is the best possible exercise; habituate yourself to walk very far." "The Europeans," he continues, "value themselves on having subdued the horse to the uses of man; but I doubt whether we have not lost more than we have gained by the use of this animal. No one has occasioned so much (as the horse) the degeneracy of the human body. Our Indians go on foot nearly as far in a day, for a long day, as an enfeebled white does on his horse; and he (the Indian) will tire the best horses."

Few, or none, perhaps, will question the abstract truth of Jefferson's observations on this point. But, because walking or progression is a "physiological" function, and the practice of it is reputed salutary, would this be, with you, a proper and sufficient reason for never setting aside or superseding in any way this "physiological" state, in the same way as you insist, on the same grounds, that the physiological pain of labour should not be set aside or superseded. Because progression is a natural condition, would this be any adequate reason for your medical advisers adopting your own arguments against anesthesia in midwifery, and insisting upon this, that, the next time you travelled from your own city of Philadelphia to the cities of Baltimore or New York, you should walk the distance on foot instead of travelling it by railway or other conveyance? What opinion would you form of the judgment of any medical adviser to whom you entrusted your own health, if, on going next time to the New York or Baltimore railway station, he should gravely and solemnly repeat to you, as his patient, what you tell your midwifery patients, and, in your own language, advise you to try to accomplish the intended journey on foot, as (to quote your own words) "a desirable, salutary, and conservative manifestation of life-force"?

Painstakingly, always in the most courteous but at the same time in the most forceful language, Simpson wrote many such letters in reply to his medical critics. These will be found reproduced in extenso in the volume of collected papers entitled *Works of J. Y. Simpson* edited by his son in a volume and published by D. Appleton & Co., New York, in 1872. I should like to quote much more extensively from them but time forbids. Let me recommend them to you for leisurely perusal.

The clerical objectors were similarly paid back in their own coin, for Simpson being a good Scots Presbyterian knew his Bible thoroughly. Here is an extract from one of his letters controverting the views of the Church on the sinfulness of abolishing the pains of labor and so nullifying God's curse on woman "in sorrow thou shalt bring forth children":

If, on religious grounds, your obstetric friends object to relieving entirely a woman of her worst pains, now that they have the means of doing so, they must, on the very same grounds, refuse to relieve her imperfectly and partially of these or any other pains and sorrows connected with parturition; they must, or at least ought to, abstain, in fact, from all obstetric practices whatsoever; they should, in short, give up their present profession as a profession of sin, and "in the sweat of their face" eat bread. I can see no other possible alternative for them, provided, that is to say, they choose to reduce actually their theory into practice. If on the other hand, they think it not sinful to relieve their female patients, to a small amount, from the alleged sufferings entailed upon them by the first curse, then surely it is not sinful in them to relieve their patients from their sufferings to a far

greater amount, now that they have the power of doing so, nay, is it not sinful in them obstinately to withhold that relief? For, "to him that knoweth to do good, and doeth it not, to him it is sin."

And if any of your female patients hold the same groundless doctrine, a doctrine far more in accordance with the blindness and fatalism of Mahommedanism, than with the spirit and genius of Christianity, if they hold that it is improper, for scriptural reasons, to abrogate the pains and sufferings of childbirth, then such mothers cannot conscientiously content themselves with rejecting merely the use of chloroform in medical assistance in their hour of travail; they must give up, indeed, all assistance whatever. If the supposed pains and perils of the primeval curse are to be submitted to, on the ground that they are divinely appointed and unavoidable ordeals, then they must be submitted to in all their unmitigated power and plenitude; no doctor must sinfully dare to stay the ebbing stream of life, if a fatal flooding suddenly supervene during labour; no nurse must venture, as heretofore, to relieve and mitigate the agonies of the shrieking mother by counter-pressure to her back, etc., "for whosoever shall keep the whole law, and yet offend in one point, he (she) is guilty of all."

It seems very strange that such arguments should have been necessary in the year 1848, not one hundred years ago. That they were necessary is shown by the number and the length of the letters which Simpson wrote. He must have covered reams of paper and have expended on them an incalculable amount of energy.

In this country he had a worthy supporter in Walter Channing of Boston. Thoms (*Walter Channing and Etherization in Childbirth*, AM. J. OBST. & GYN. 20: 244) has recently written a short memoir of him pointing out how Channing played the same part in answering medical, lay, and clerical criticism here as did Simpson in Scotland.

Both of them had the satisfaction before they died of knowing that their efforts had not been in vain.

It is always interesting to try to picture the physical make-up of men who have had their names written upon the Book of Fame. Numerous photographs and portraits of Sir James Young Simpson exist. He was described, somewhat fulsomely, by a contemporary as follows:

In stature the Professor is somewhat under the middle size. The roundness of his whole form and the absence of Scotch "processes of bone" would authorise the inference of English extraction. His ambrosial locks, dark and almost imperceptibly shaded with red, fall upon his shoulders. No feature in the Professor's countenance is overgrown. The forehead is broad and projecting rather than lofty. There is much firmness about the mouth and the lips. The eye is brilliant, and looks out from the eyebrows with an energy and penetration betraying great mental power. With the fiercer radiation of its eagle fires is blended the soft glow of a warm heart, which gives it a decided intellectual and moral expression. There is a fascination in his air, manners, and conversation, an irresistible moral gravitation which elicits and wins the admiration, love, and confidence of all who come within the magic circle of its influence.

A medical colleague wrote in 1848:

Decidedly the most wonderful man of the age in which he lives is Simpson of Edinburgh. Nothing baffles his intellect, nothing escapes his penetrating glance, he sticks at nothing, he bungles nothing. From all parts, not of Britain only, but of Europe, do ladies rush to see, consult, and see the little man.

Another described him as possessing "the head of Jove, the body of Bacchus."

And so I confess that I am sentimental enough to be a hero worshiper and to feel that we can derive inspiration and courage from a reperusal of the lives of great men. Such study teaches us that dry-as-dust knowledge is not everything. The great physician, the great surgeon must of necessity be more than a scientist or a technician. He must have that something which we call personality, and he must have interests outside those of his calling. So it behooves us to take care that our present hidebound regulations for the admission to the study of medicine, and our rigid scientific curricula do not exclude and do not dampen the enthusiasm of some who, if given the opportunity, might develop into great clinicians.

ANEMIA IN PREGNANCY

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INNUMERABLE reports have been published about the etiology and treatment of anemia in pregnancy. Some investigators have reported improvement but none, so far as we know, have reported failures with various types of therapy. The frequency of anemia in pregnancy in a large series of patients should be determined and notation made of what happens if these same patients are not treated and what the results are if they are treated.

Various types of anemia occur during pregnancy. The first and most common is the so-called "physiologic anemia" of pregnancy. This is demonstrated by the curves shown in Fig. 1, which represent hemoglobin and cell volume determinations obtained during pregnancy by various investigators. The different figures given for hemoglobin have been recalculated to a standard of 100 per cent, containing 14.3 gm. per 100 c.c. Kühnel, in a serial study of the same 15 patients during pregnancy and the puerperium with carefully controlled methods, concluded that there is a gradual drop in hemoglobin, cell volume and erythrocyte count until the sixteenth to twenty-second week. This low level is maintained until about the thirtieth to thirty-second week when these substances begin to increase but reach a figure at thirty-four to thirty-six weeks which is lower than the initial figure. The hemoglobin concentration is not normal until weeks and occasionally months after delivery. Curve 2 in both figures is taken from his work.

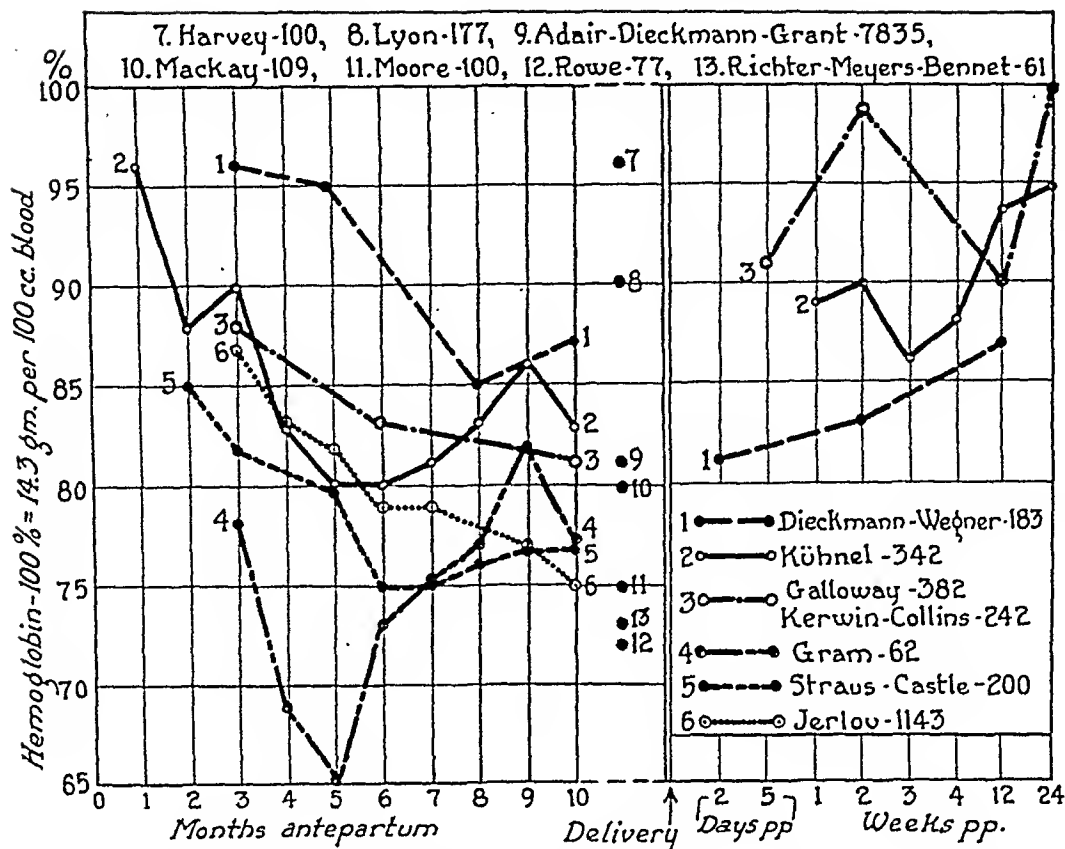


Fig. 1-A.—Graph illustrating the hemoglobin curves in pregnancy as reported by various investigators.

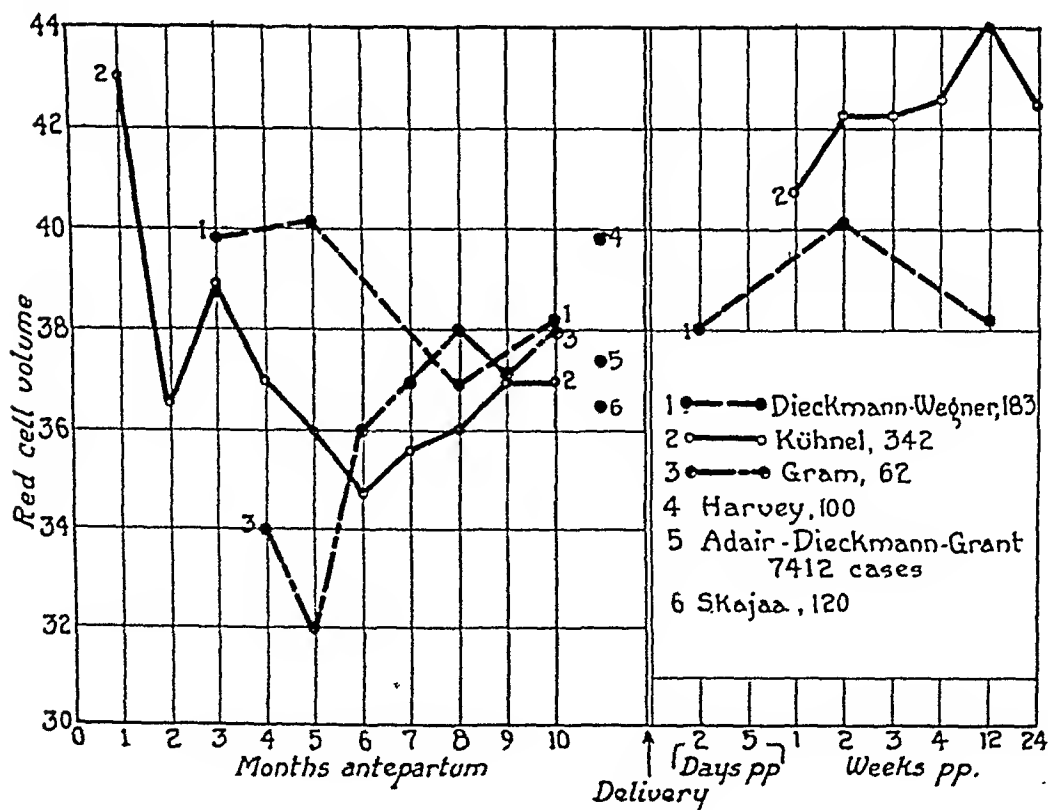


Fig. 1-B.—Graph illustrating the cell volume curves in pregnancy as reported by various investigators.

Dieckmann and Wegner (curve 1 in Fig. 1), like Kühnel, followed the *same* patients during pregnancy and the puerperium. Determinations of blood and plasma volumes and exact determinations of hemoglobin, cell volume and cell counts were made at periodic intervals. They concluded that at term the blood volume shows an average increase of 23 per cent, the plasma of 25 per cent, and the total erythrocyte mass of 20 per cent. This discrepancy of 5 per cent accounts for the decrease in hemoglobin concentration, cell volume, and erythrocyte count seen in normal pregnancy. This phenomenon is termed the "physiologic anemia."

They further found that there is an average decrease in the hemoglobin concentration in normal pregnancy amounting to 15 per cent at twenty-five to thirty-five weeks. From then on until term, the hemoglobin increases and may reach a normal level. They reported that the total amount of hemoglobin showed an average increase at term of 13 per cent, but this increase in hemoglobin is less than the increase in blood volume. They stated that many of the previously reported figures for hemoglobin, cell volume and erythrocyte counts in pregnancy are in many instances at variance with each other and the results are inconclusive because, with but few exceptions, the determinations were made with methods and apparatus which were not standardized and the *same* women were not followed throughout pregnancy. Wintrobe, Haden, and Osgood and Haskin in a careful study of nonpregnant women have shown that the lower limit of normal for the hemoglobin concentration is 12 gm. Dieckmann and Wegner concluded from their work that in pregnancy the lower limit of normal is 10 gm. per 100 c.c. of blood. They also showed, and apparently for the first time, that during pregnancy there are marked individual variations in the same women of all of the indexes, especially of the color indexes, but the average for each remains close to one. In the study of the individual cell, they found that the corpuscular volume is increased slightly between the twenty-sixth and thirty-fifth week when the physiologic anemia is most marked. The corpuscular hemoglobin is increased slightly both in amount and in percentage during the greater part of pregnancy, but it is normal at term and during the puerperium. The hemoglobin and the volume coefficients are increased during the greater part of pregnancy, but they are essentially normal at term and during the puerperium. They stated that the amount of hemoglobin per kilogram of body weight increased slightly during pregnancy.

A second type of anemia in pregnancy occurs in women who have a subnormal hemoglobin in early pregnancy and when the "physiologic anemia" occurs, the drop in hemoglobin is so great that symptoms and signs of anemia occur, which may clear up after delivery or may persist. This is usually a microcytic type of anemia with the corpuscular volume ranging between 70 to 80 cu. μ . This group forms the vast portion of anemia in pregnancy, and the patients as a rule have no symptoms or signs of the condition.

Strauss and Castle examined the gastric juice, both fasting and after a test meal, and determined the hemoglobin concentration in a number of pregnant women. They concluded that 18 out of 24 or 75 per cent of their patients showed an acid secretion below the normal range during more than one-half of the period of pregnancy. They also concluded that the anemia of pregnancy (not the physiologic type which they thought was probably due to a hydremia) which occurs during the last trimester of pregnancy, is due to the demands of the fetus for blood-forming substances, and "is found only in those patients who have had for a considerable time a defective diet or dietary deficiencies conditioned by gastric anacidity or related gastrointestinal disturbances." They stated that the

hypochromic anemia of pregnancy could be relieved, *without exception during pregnancy*, by the daily administration of 6.0 gm. of iron ammonium citrate. This conclusion is based on studies made on 30 patients with the hypochromic microcytic anemia and 6 with the macrocytic anemia.

A third type is rare and is characterized by a larger cell, ranging from 90 to 130 cu. μ . These patients usually have symptoms and signs of anemia and at times seem to have a toxemia of pregnancy as indicated by edema and albuminuria. The blood smears show all the characteristics of a pernicious anemia and occasionally the differential diagnosis is difficult. As a rule, there are no neurologic findings and the characteristic increase in reticulocytes does not occur after administration of liver. Such patients were formerly designated as having pernicious anemia of pregnancy. The mortality rate was quite high, and it was probably such patients who were described by Channing and Osler.

An anemia occurring in pregnancy with a maternal mortality of 40 per cent and a fetal one of 63 per cent has been repeatedly described in Indian medical journals. This anemia has been reported in both men and women, but its greatest incidence is in pregnancy. Recovery does not take place until after delivery, when it may occur spontaneously. The anemia is due to a deficient diet as Wills has demonstrated that the feeding of marmite (brewer's yeast) will cure the disease. Furthermore, she has been able to produce a similar anemia in monkeys by eliminating protein and yeast from their diet and to cure it by feeding them these substances.

An editorial was published in the *Indian Medical Gazette* for 1932 which gives not only the history of anemia of pregnancy but also summarizes all of the Indian reports. The "Indian" anemia occurs in 2.93 per cent of their hospital deliveries. The onset is usually abrupt and occurs between the fifth and seventh month of pregnancy. Balfour found that one-half of the patients had an initial fever and 83 per cent had fever some time during the disease. Most of the cases occur between October and March. Seventy-five per cent of the women are between fifteen and twenty-nine years of age. A third of the cases occur in the first pregnancy and another third occur in the second and third pregnancies. The patient's skin is pale, flabby and looks edematous. Tachycardia, dyspnea, vomiting, diarrhea, weakness, sore mouth, albuminuria, edema, hypotension, palpable liver and spleen are the usual symptoms and signs. The gastric juice contains free HCl and is normal in all respects. Bacteria are quite commonly found in the urine. The average erythrocyte count is 1,210,000, the hemoglobin is 33 per cent and the color index is 1.4. Anisocytosis, poikilocytosis and some polychromatophilia, normoblasts and megaloblasts are noted in the blood smears. Postmortem examination reveals very pale organs containing free iron.

Labor is an added risk. There is exceptionally little blood loss during the third stage, but labor is apparently too much of a strain on the heart because 21 per cent of the patients die during delivery or within the first week postpartum. The babies are small, usually weighing less than 5 pounds. Their hemoglobin is normal at birth.

A therapeutic abortion should be performed if the patient is seen in the first three months. Since the disease as a rule does not occur or is not noticed until later in pregnancy, the treatment is entirely medical. A proper diet with the

addition of liver and marmite (yeast) should be instituted. Twenty c.c. of blood injected intramuscularly once or twice a week appears to be of value. Blood transfusion apparently starts labor and is therefore contraindicated. While the disease does not seem to recur, future pregnancies should be prevented.

METHOD

Blood was taken from an arm vein without stasis and heparin was used as an anticoagulant. The cell volume was determined by centrifuging the blood in Wintrobe hematocrit tubes for a period of one hour at 3,600 r.p.m. The amounts of hemoglobin were determined with a Newcomer pipette and colorimeter, using a glass color plate and blue filter. The plate was standardized by the oxygen capacity method and found to need no correction. Duplicate hemoglobin specimens were usually analyzed in the chemical laboratory every two weeks with a carbon monoxide method. Erythrocyte counts were made with the usual technic but the chambers and pipettes were standardized against a chamber and pipette certified by the Bureau of Standards. The cell volume method has a maximum error of 2 per cent. The Newcomer method, with an exact technic, has an error of 5 per cent, but with the usual technic entailed in a clinic laboratory in which as many as 75 to 125 patients daily were examined by two technicians, the possible error was 8.7 per cent. Likewise, the possible error in the red cell count in the clinic laboratory amounted to 13.7 per cent, while the same technician with careful technic which was time consuming could reduce the error to 2 per cent. The error in the cell volume was not affected by the number of patients examined and is the most foolproof of the three determinations. All determinations have been made by three technicians and no change was made in technic at any time.

Various observers have shown that the hemoglobin, cell volume and cell count, although constant for the individual, do fluctuate during the period of a day. The hemoglobin may fluctuate as much as 15 per cent (2.07 gm.) and the cell volume and erythrocyte each 3 and 17 per cent, respectively. Thus in attempting to determine the value of any medication, one has to take into account the inherent error of the determination, the normal curve of hemoglobin in pregnancy as well as the hourly fluctuations of hemoglobin.

Our statistical data are summarized in Table I. Series I comprises all pregnant patients admitted during the period from March, 1932, to March, 1934; Series II, the period from March, 1934, to November, 1935. The total series is composed of I and II. The private group consisted of all patients who were delivered by members of the department staff during 1934. The gynecologic group was composed of all nonpregnant patients, excluding only those who had been pregnant within three months.

Series I and II were studied separately because they check against each other, since there was no change in technic or personnel during the four-year period. It is of interest that for the total series the average hemoglobin is 11.56 as com-

pared with that of Dieckmann and Wegner of 12.5; that the mean cell volume is 37.31 as compared with that of 36.9, and the mean erythrocyte count is 3.77 as compared with that of 4.20.

In Fig. 2 *A*, *B*, and *C* are shown the frequency distribution of the hemoglobin, cell volume, and red cell count. It is obvious that the maximum number of cases fall in the groups with 10, 11, and 12 gm. of hemoglobin and in the 35 to 44 volume per cent groups for the cell volume and the 3.40 to 4.19 groups for the red cell count. These average frequencies for the various substances are decidedly less than those reported for the nonpregnant woman.

Fig. 3 is a frequency graph in which the hemoglobins for various groups of patients are compared. It is obvious that the greater number of gynecologic patients, even with obvious anemias included, fall in the 11, 12, 13, and 14 gm. groups. In this group 1.5 per cent were under 8.0, 3 per cent were under 9.0,

TABLE I. SUMMARY OF THE STATISTICAL DATA

	ALL PREGNANT PATIENTS			PRIVATE OBSTETRIC PATIENTS 1934	ALL GYN. PATIENTS 20 MO.
	SERIES I 24 MO.	SERIES II 20 MO.	TOTAL SERIES 44 MO.		
<i>Hemoglobin—Gm. Per 100 c.c. of Blood</i>					
Number of patients	4,342	3,493	7,835	170	2,399
Mean \pm	11.42	11.76	11.56	11.79	12.76
Probable error	>0.001	>0.001	>0.001	0.065	>0.001
Standard deviation	1.4	1.4	1.4	1.26	1.68
Range			4.0-16.9	8.0-15.9	4.0-16.9
<i>Cell Volume—Volumes Per Cent</i>					
Number of patients	4,168	3,528	7,696	135	1,227
Mean \pm	37.4	37.2	37.31	38.46	40.76
Probable error	>0.01	>0.01	>0.01	0.218	>0.01
Standard deviation	4.2	4.2	4.2	3.76	5.07
Range			15-54	25-49	15-54
<i>Erythrocytes—Millions</i>					
Number of patients			4,345	168	
Mean \pm			3.77	3.801	
Probable error			0.001	0.0195	
Standard deviation			0.405	0.375	
Range			1.60-5.00	2.80-5.00	

5.8 per cent were under 10, 11.7 were under 11, and only 25.8 were under 12. Comparable figures were obtained for cell volume and cell count. In contrast among the total group of pregnant patients 1.5 per cent had hemoglobin readings under 8.0 gm., 4.3 per cent were under 9, 11.6 per cent were under 10, 31.3 per cent were under 11, and 63.2 per cent were under 12 gm. In the group of private pregnant patients none had a hemoglobin less than 8 gm., only 1.2 per cent were under 9, 7 per cent were under 10, 25.9 per cent under 11, and 55.3 per cent under 12. Naturally, comparable figures were obtained for cell volume and cell count. While the difference between private and clinic patients is not a significant one, yet we believe that there are probable nutritional and hygienic factors in these anemias. There is no doubt that there is a significant difference between non-pregnant and pregnant patients and that pregnancy, in a corresponding stratum of patients, lowers the hemoglobin at least relatively.

One group of patients with anemia was given 5 gm. of ferrous carbonate daily, another group was given 5 gm. of iron ammonium citrate daily, another group was treated with blood transfusion, either after medication had failed or there was insufficient time before delivery for medication to have any effect. Other groups were treated with various other iron salts and with various proprietary

preparations, and lastly a control group was given no treatment. The period of observation and treatment with iron medication was at least four weeks and preferably twelve weeks. Due to the number of cases studied, and a small personnel, the follow-up was inadequate, and while there is a small number of carefully controlled patients, we do not believe that the results of treatment can be stated with certainty. There are sufficient data to indicate that it is extremely difficult to evaluate any medication over a period of weeks while the patient is pregnant because of the uncertainty of the normal curve of hemoglobin in pregnancy. We are discussing only the effect of treatment during pregnancy, because

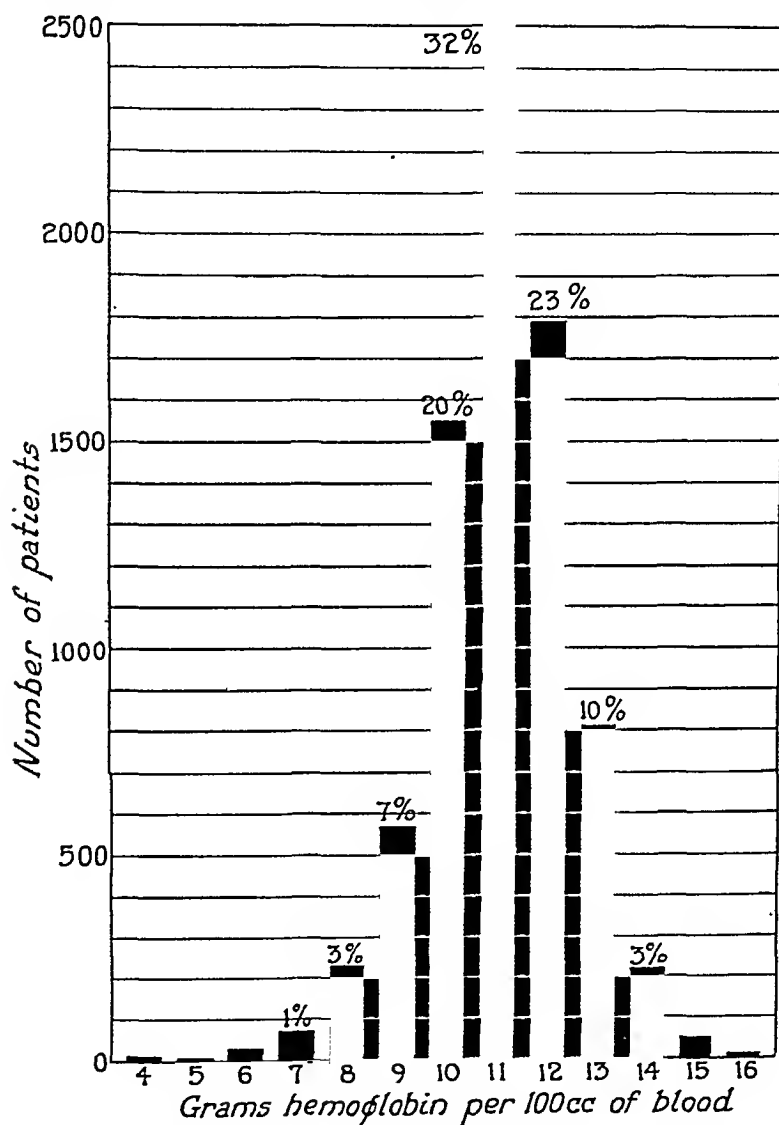


Fig. 2-A.—Graph illustrating the frequency distribution for hemoglobin (7,835 patients).

after delivery the hemoglobin will naturally tend to return to normal or the administration of iron will result in improvement in almost every case.

Table II lists the changes in hemoglobin concentration during pregnancy. The patients in column A were normal pregnant women; 9 out of 14 showed varying decreases in hemoglobin during pregnancy; 10 of these same patients without any treatment showed comparable increases after delivery of the same magnitude as the antepartum diminutions.

All other patients had a hemoglobin concentration of less than 9.0 gm. per 100 c.c. of blood on two occasions within a period of one to two weeks. Column B

indicates what happened to a group of anemic patients who had no treatment. Sixty-five patients showed varying amounts of increase in hemoglobin during pregnancy, 6 showed no change and 3 showed a still further reduction in hemoglobin. In 26 patients the anemia disappeared after delivery without treatment while 5 patients showed further decreases in hemoglobin.

Data from patients who received ferrous carbonate appears in Column C; from those who received iron ammonium citrate in D, and those who received a proprietary preparation which contained iron, liver, and vitamin B in Column E.

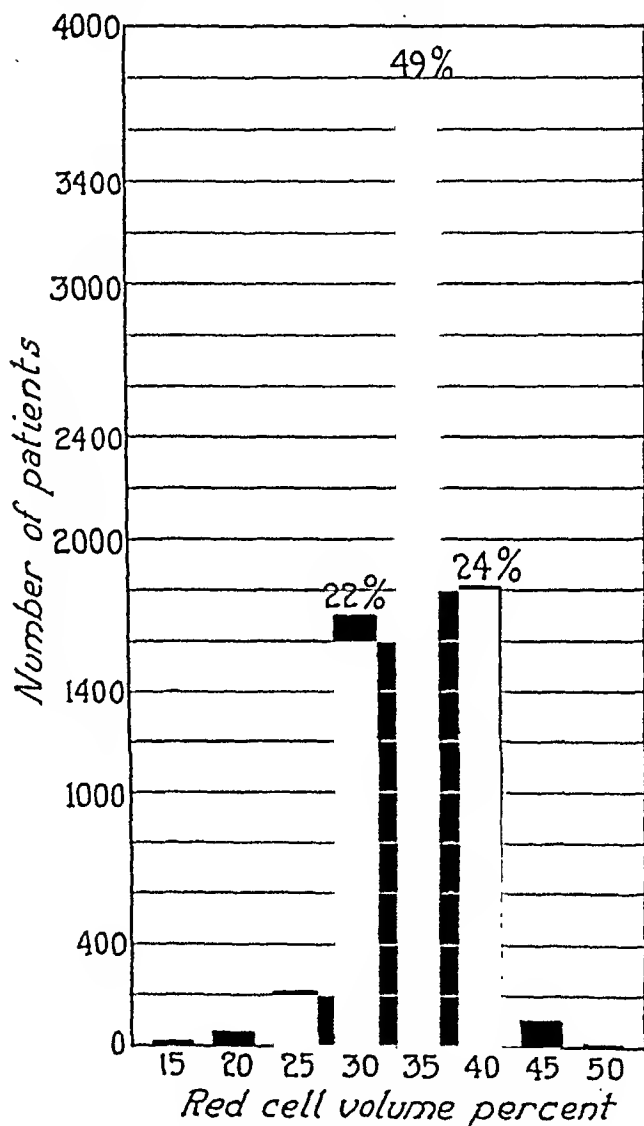


Fig. 2-B.—Graph illustrating the frequency distribution for cell volume (7,696 patients).

It is obvious that the majority of the patients in each group showed varying degrees of increase in hemoglobin concentration during pregnancy, a few showed a further decrease and some, especially those receiving ferrous carbonate, showed no change. No significant differences in the increase of hemoglobin concentration in Columns C, D, and E as compared with B can be demonstrated.

Column F contains data from a number of anemic patients who were transfused before delivery and others who were transfused after delivery. In both groups, but especially the latter, transfusion was necessary because treatment with iron salts had been of no value. Hemorrhage had not been the cause of

the anemia in the antepartum group but was the cause of a persistent anemia in several of the postpartum cases. It is evident that if an adequate amount of blood is given, a prompt and usually permanent increase in hemoglobin concentration occurs.

Studies of 79 cord bloods were made in cases where the maternal hemoglobin was or had been below 9.0 gm. during pregnancy. The means for this group for hemoglobin, cell volume and cell count were 16.21 gm., 53.85 and 4,128. The figures for a normal group of cord bloods were 16.81, 50.94, 4,488. There is no significant difference.

Fig. 4 contains essential data from patient No. 73027. The patient was thirty-four years old and had three living children. She had a severe secondary anemia of pregnancy. She received adequate amounts of ferrous carbonate and an anti-

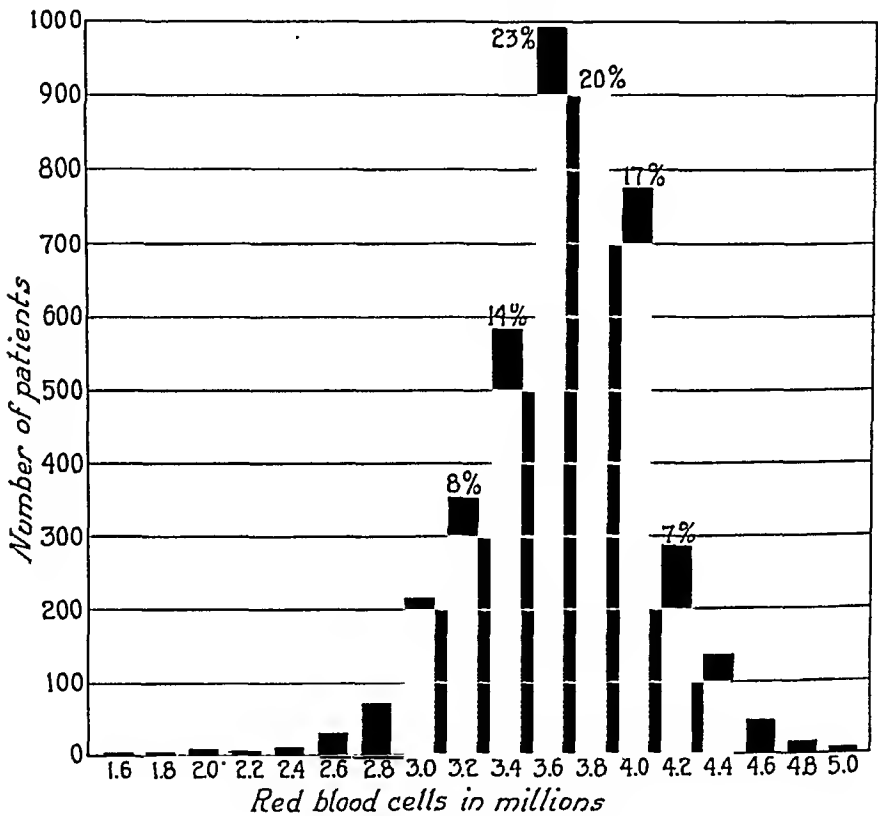


Fig. 2-C.—Graph illustrating the frequency distribution for erythrocytes (4,345 patients).

anemic diet. No increase in hemoglobin concentration occurred until after delivery. Iron metabolism studies showed a slight positive balance on diet but when ferrous carbonate was given the balance became negative. This patient had a color index of 1.05 to 1.17 and volume index of 1.20 to 1.26. The corpuscular volume was 104 to 108 cu. μ . Anisocytosis, poikilocytosis, and macrocytes were present throughout pregnancy. Her blood volume was always a low normal but what is of more importance the amount of hemoglobin per kilo was very markedly below normal. Repeated gastric analysis showed no free HCl in the fasting contents. After the injection of histamine a small amount of free HCl was present. The labor and delivery were uneventful. The baby weighed 3,985 gm. In view of the patient's age and the desirability of preventing further pregnancies and blood loss during menstruation, the uterus was removed. During pregnancy the iron content of the diet was sufficient for a positive balance but the fetal need of 4 or 5 mg. per day was lacking. On an intake containing 17 times the optimum

amount which was 20 mg. the patient was not in balance and the hemoglobin concentration did not increase. The infection had subsided before the latter study was started. There were repeated determinations of the iron balance but data from only three periods are given.

Fig. 5 contains essential data from patient No. 54736. She was twenty-five years old and this was her first pregnancy. She had been told seven years previously that she was anemic. She was admitted to the hospital because of diarrhea, abdominal cramps, vomiting, sore mouth, edema and anemia. Her color index was 1.06 to 1.14 and volume index 1.00 to 1.08. The corpuscular volume was

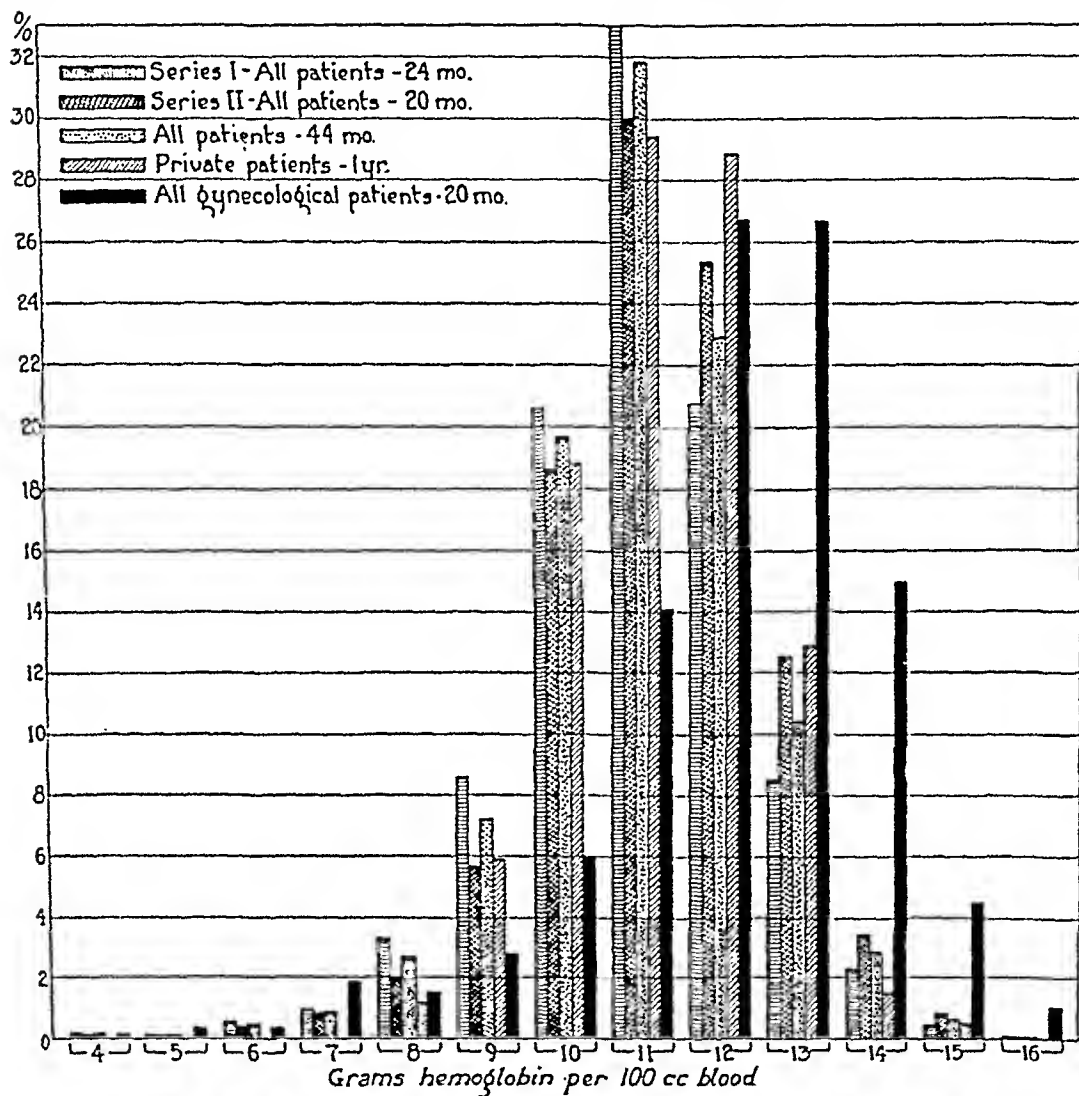


Fig. 3.—Graph illustrating the comparative frequency distribution for hemoglobin.

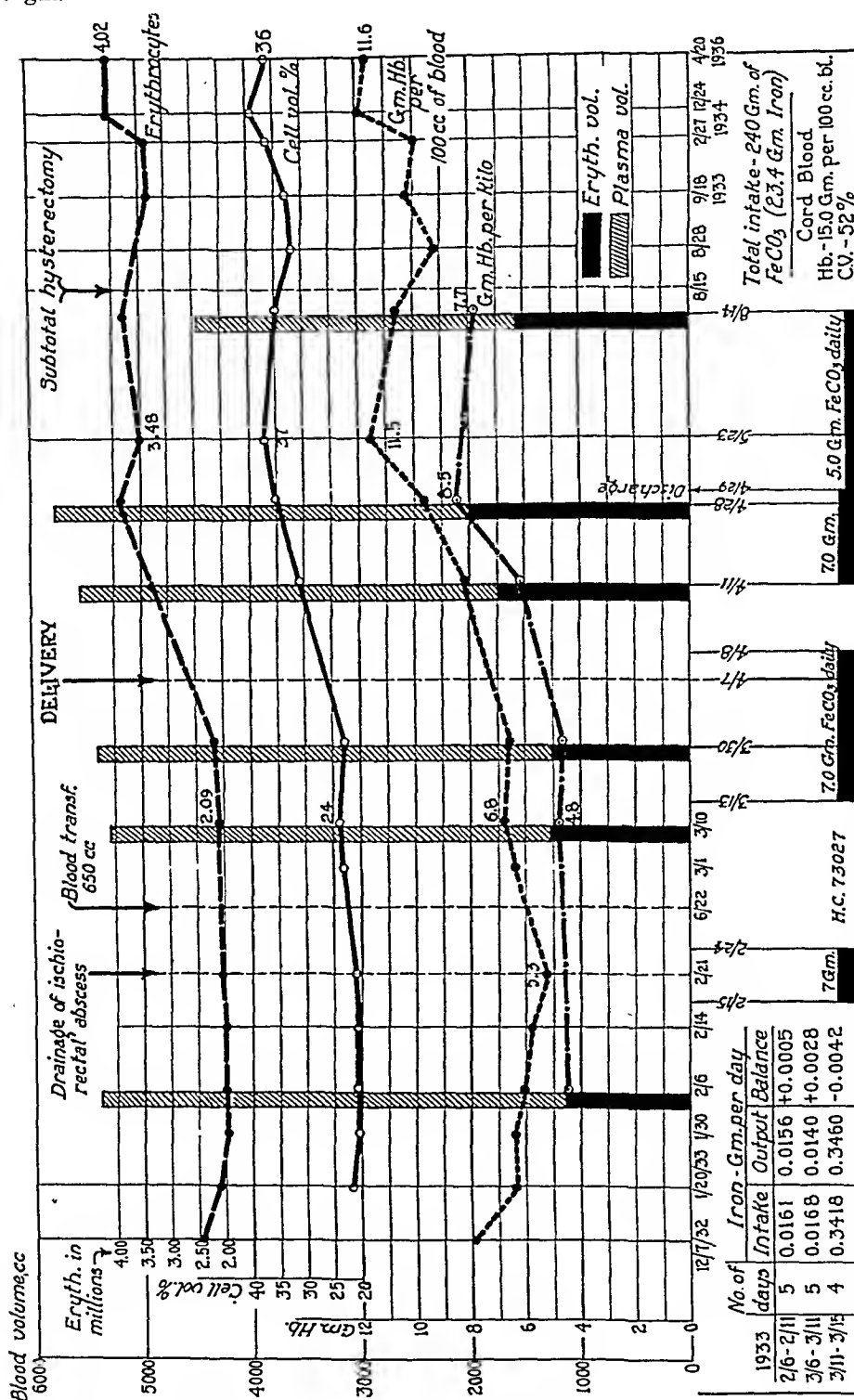
90 cu. μ . The usual type of abnormal cells were found. The hematologist was suspicious of a pernicious anemia but in view of free HCl in the fasting gastric juice, absence of neurologic findings and failure of parenteral liver extract to cause a characteristic increase in the reticulocytes, the final diagnosis was grave secondary anemia of pregnancy. The low blood volume and especially the very small amount of hemoglobin per kilo are noteworthy. She was given 4,600 c.c. of citrate blood over a period of twenty-three days. This was sufficient to raise the hemoglobin concentration and hemoglobin per kilo to normal, and give her a normal blood volume. She has never received any other antianemic medication and

TABLE II*

CHANGE IN HEMOGLOBIN GM. PER 100 G.C.	DIECKMANN-WEGNER NORMAL PREGNANT WOMEN										ANEMIA AND TREATMENT DURING PREGNANCY									
	A				B				C		IRON AMMONIUM CITRATE		LIVER IRON AND VIT. B		TRANSFUSION INCREASE					
	ANTEPARTUM		POSTPARTUM		UNTREATED		POSTPARTUM													
	+	-	+	-	+	-	+	-	+	-	+	-	+	-	ANTE- PARTUM	POST- PARTUM				
0.1-0.4	1	1	2	1	8	1	1	1	1	2	1	1	1	1	1	1				
0.5-0.9	1	1	4	1	15	2	1	3	3	3	3	6	2	1	1	1				
1.0-1.9	1	1	3	1	21	2	3	3	14	3	11	2	3	5	1	1				
2.0-2.9	1	2	3	1	15	3	4	4	12	8	8	3	1	1	2	2				
3.0-3.9	1	2	1	1	3	2	5	2	8	4	5	2	1	1	4	4				
4.0-4.9	2	2	1	1	1	2	2	2	4	2	2	1	1	1	1	1				
5.0-5.9	2	2	1	1	1	2	2	2	4	2	2	1	1	1	1	1				
No change	2	1	1	1	6	6	6	6	13	13	3	4	4	9	9	9				
Total patients	14	14	14	14	74	31	31	31	60	60	35	17	17	9	9	9				

* (+) indicates increase and (-) indicates decrease in hemoglobin concentration.

despite a slight polymenorrhea her hemoglobin has remained normal over a four-year period. She has been using contraceptive measures. The baby weighed 3,380 gm.



symptoms and signs disappeared and the remainder of the pregnancy was uneventful in three. Two patients were subsequently delivered of twins. The fourth patient had a premature delivery of a macerated fetus three months after the transfusion. Three years later she again had a premature stillbirth in another

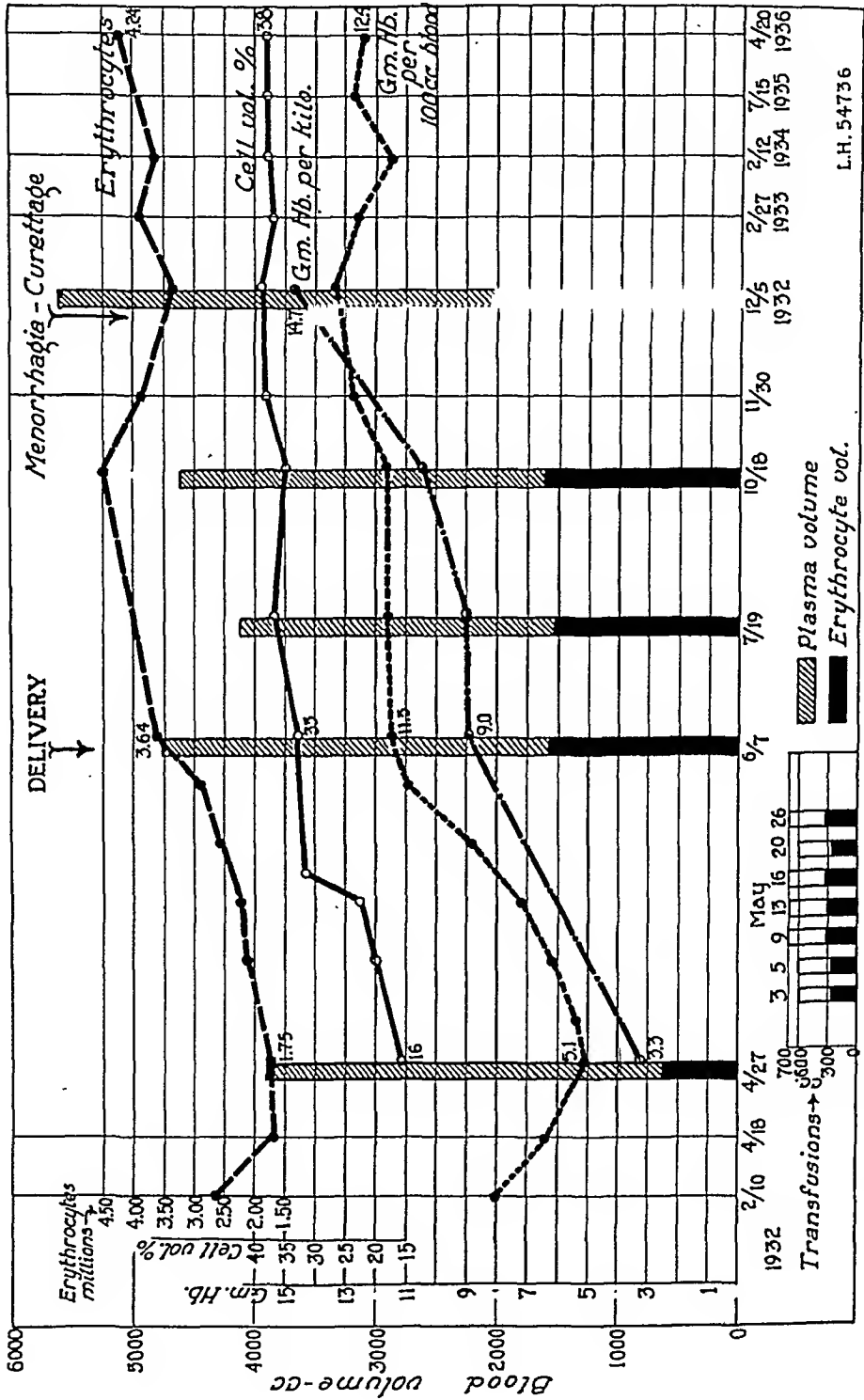


Fig. 5.—Graph of patient with severe anemia of pregnancy who was treated with blood transfusion.

hospital and when seen four months postpartum had a hemoglobin of 6.8 gm. per 100 c.e., cell volume of 28, and cell count of 3,840,000. She states that there was no appreciable hemorrhage. Consequently the pregnancy may have caused the anemia which in turn may have produced the premature labor.

Dieckmann has given the following average figures for the hemoglobin concentration of 38 patients with preeclampsia as 12.9, for 59 patients with vascular-renal disease as 13.2, and for 34 patients with eclampsia as 14.9 gm. per 100 c.c. The average figures for the cell volume are 38.6, 40, and 45 volumes per cent, respectively. While these figures may be higher than they should be because of the blood concentration found in preeclampsia and eclampsia, yet they indicate that the majority of the acute toxemias of pregnancy seen by us are not due to or associated with an anemia.

There were 906 patients with anemia over a period of three years eight months. Only 2 deaths occurred during this period in which the chronic anemia was a possible factor. Both patients had edema, albuminuria, dyspnea and weakness, and in both these symptoms were attributed to cardiac decompensation. Post-mortem examination revealed that one did have cardiac disease but the other autopsy did not show any pathology sufficient to account for death. The pathologist noted in both cases that the tissues contained less blood than normal.

DISCUSSION

Many obstetricians have stated that chemical analysis of the blood in pregnancy is of little value. The importance of at least one application of chemistry to obstetrics is illustrated by the fact that chemical determination of hemoglobin, a complex chemical compound, indicates that 63 per cent of our pregnant women are anemic according to nonpregnant standards.

Our data indicates that the concentration of hemoglobin, the cell volume and the erythrocyte count are definitely decreased during pregnancy and that the normal standards for the nonpregnant differ from those of the pregnant women. Our average figures are slightly less than those of Dieckmann and Wegner, and Kühnel, because patients with marked anemia are included in our tables. Statistically the minimum figures in normal pregnancy should be 10.16 for hemoglobin, 33.11 for cell volume and 3.36 for erythrocyte count.

Dieckmann and Wegner postulated that the decrease in the erythrocytes was a part of the mechanism by which the viscosity of the blood was lowered. This phenomenon, according to them, in combination with an increase in the blood volume corresponding to an increase in weight, a decrease in serum protein concentration and increase in cardiac output are necessary for the gaseous metabolism of the fetus and also of the maternal tissues and tend to minimize strain on the cardiovascular system of the mother.

The physiologic decrease and increase in hemoglobin, cell volume and erythrocytes during pregnancy have not been properly evaluated by investigators. The fact that the hemoglobin concentration can increase 2, 3 or even 6 gm. within four weeks without treatment at once casts doubt on any reports which state that improvement occurred during pregnancy when iron salts were administered.

It is our belief that the hemoglobin concentration of the cord blood is usually normal even though the mother has an anemia, but in a num-

ber of instances the hemoglobin concentration has been definitely below normal. This is especially important in view of the fact that milk contains little iron and if the baby begins life with a low concentration of hemoglobin, anemia is quite likely to develop. Recognition of the above is most important in premature infants because they are born without the storage of iron in the liver which exists in the term baby. Furthermore severe anemia predisposes to premature delivery.

Transfusion of blood, if properly supervised and if adequate amounts are given, has always been efficacious in raising the hemoglobin concentration and relieving all symptoms and signs of anemia. Deleterious effects on mother and baby have not been observed and premature labor was in no case initiated.

A number of iron metabolism studies have been made in both nonpregnant and pregnant individuals. Farrar and Goldhamer kept two subjects in a positive balance on a daily intake of 5.2 and 7.8 mg. of iron, respectively. The period of study was 316 and 260 days, respectively. Females require more iron because at least 12 mg. of iron are lost in the form of hemoglobin during each menstrual cycle. Ohlson and Daum report that an average daily intake of 13.8 mg. of iron resulted in a negative balance.

Coons and coworkers have reviewed and studied the iron metabolism during pregnancy. They have shown that with an average daily intake of 14.72 mg. there will be an average positive daily balance of 3.16 mg. A 3,100 gm. fetus will contain approximately 375 mg. of iron. The fetal need for iron first becomes noticeable at twenty weeks, but it rapidly increases and at term it requires 8 mg. per day. During the last trimester of pregnancy the average daily requirement for the fetus is 4.7 mg. Coons concluded that "iron retention was found to be quite deficient in this series of metabolic studies. There were no negative balances but approximately three-fourths of the number fell short, many of them far short of the estimated fetal need. The low retentions were not due to low total iron intake but probably to a deficiency of other dietary factors which promote the utilization of iron."

It is obvious that if the cause of the anemia occurring in pregnancy is merely a lack of iron in the diet then these patients who receive iron should all show rapid improvement if adequate amounts of iron are added. The fact that a considerable number of patients show no improvement indicates that some other substance is lacking or that the iron is not being absorbed or that if absorbed it is not being utilized.

CONCLUSIONS

The means for the hemoglobin concentration in pregnancy are 11.56 gm. per 100 c.c. of blood, for the cell volume 37.31 volume per cent, and for the erythrocyte count 3.77 million.

The minimum standards for normal pregnancy are 10 gm. of hemoglobin per 100 c.c. of blood, 33 volumes per cent for the cell volume, and 3.36 million for the erythrocytes.

Eleven and six-tenths per cent of our pregnant patients have an anemia, according to our standards, but if the standards for the non-pregnant patients are used 63.2 per cent must be classed as anemic.

A normal decrease and increase in the hemoglobin, cell volume and erythrocyte count occurs during pregnancy. These changes cannot be altered by treatment. The fluctuation may amount to 2, 3 or even 6.0 gm. of hemoglobin within a period of four to six weeks.

Knowledge of these marked fluctuations should make one particularly cautious about attributing an increase in the hemoglobin concentration, cell volume and erythrocyte count to any previous therapy.

An adequate amount of transfused blood will raise the hemoglobin concentration to normal permanently and relieve all the symptoms and signs of the anemia.

Blood transfusion during pregnancy, if done properly, has no deleterious effect on the mother or the fetus. It has not caused premature labor.

The prevention of anemia of pregnancy is easier than the cure. An adequate diet, with proper hygiene, is the best prophylaxis.

A normal hemoglobin content is essential for the normal function of the organs of the body. Toxemia is less likely to occur, the patient is better able to tolerate blood loss and the strain of labor, her tissues have more resistance, she is less likely to become infected, and her recovery after delivery is more rapid.

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DISCUSSION

DR. FRED L. ADAIR, CHICAGO, ILL.—Dr. Dieckmann and Dr. Grant have carried on most of the detail work in connection with this study which had as its fundamental concept the idea that there were certain physiologic changes in the blood during pregnancy which indicated an anemia. We were dealing in many cases with an anemia which was not a true anemia and certain standards had to be established which were somewhat different from those for the nonpregnant woman. We have attempted to follow patients on a higher economic level, who it was supposed had better hygienic conditions than our other patients. We also used as a control

group the gynecologic cases. I would like to stress the fact that we were dealing with all gynecologic conditions, and in spite of many cases that had definite secondary anemia from uterine bleeding, there was still a significant difference between the blood condition of these and the pregnant patients. We distinguished, then, between what may be called a physiologic or a relative anemia and an actual anemia which unquestionably does exist in some of the pregnant women.

Now, so far as to what constitutes actual anemia we believe that the standard for pregnant women should be a gram or more lower than for the nonpregnant. In other words, if you assume that 12 gm. is the normal limit, you should probably take 10 or 11 gm. as the lower limit for pregnancy. On this basis we found that in our private patients only 7 per cent had a hemoglobin below this level of 10 gm., whereas in the clinic cases there were 12 per cent. We assume the discrepancy is largely due to the difference in hygiene and in nutrition. According to our observations so far, diet and hygiene are of far more importance than any medication that can be given.

Among all of our gynecologic patients, which include some with genital bleeding, we find that 74 per cent had a hemoglobin of 12 per cent or above. If we include all cases, only 37 per cent were over 12 per cent, so that there is a very significant difference in the hemoglobin. Then, if we take the private prenatal cases, we find that 45 per cent were over 12, whereas in the clinic cases 37 per cent were over 12. We conclude, therefore, that so far as anemia is concerned there is first, a physiologic condition of the blood which simulates anemia in the nonpregnant woman; second, that our private patients have less actual anemia than clinic patients; third, that nonpregnant women show an actual anemia less frequently than the pregnant women, due to the different accepted standards.

We also made a study of the fetal blood. Apparently the fetus has few iron requirements until after twenty weeks of gestation, after which time the daily requirement for iron gradually increases until at term it reaches a point of 8 mg. We would say, then, that prior to twenty weeks of gestation the demand on the part of the fetus for iron is not appreciable. We studied fetuses born of mothers with anemia, taking 6, 8, and 9 gm. as a basis for our estimate. The average hemoglobin in these cases was 16.2, the erythrocyte count reading a little less than a quarter million. In the control cases we found that the hemoglobin readings were essentially the same, 16.8 as compared to 16.2; the erythrocyte reading was a little less than four and a half million, showing a little higher hemoglobin reading in the control series and a little higher erythrocyte count. Probably the hematocrit reading was a little higher than the erythrocyte reading and the hemoglobin.

We feel, then, that the anemia condition in the mother has little influence on the fetus so far as the blood findings are concerned. If the fetus is born prematurely it has a relatively small amount of iron, whereas the full-term fetus has stored considerably more iron. We believe from these observations that most of the iron supply takes place in the last six weeks. This is undoubtedly a handicap for the premature fetus.

DR. EVERETT D. PLASS, Iowa City, Ia.—I would like to ask whether the authors feel that there is any relationship between the amount of protein in the diet and the tendency of pregnant women to develop anemia?

DR. DIECKMANN (closing).—In reply to Dr. Plass, we cannot stato definitely but we believe that diet is the prime factor in the anemia of pregnancy. Certainly this is true in the anemias which occur in India, and as Dr. Adair emphasized, the difference between our ward and private patients is probably due to the difference in diet. The important part of the diet being the protein which, of course, unfortunately is the more costly of the various foods.

A FURTHER STUDY OF EXTRAPERITONEAL PELVIC CONDITIONS IN WOMEN

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EXTRAPERITONEAL pelvic conditions, although not of frequent occurrence, are met with sufficiently often to deserve more attention than is usually given them. In 1930 I published an article on this group of lesions and today I shall discuss this subject more thoroughly, adding to the series reported in the first paper some cases seen since 1930 which demonstrate additional types of extraperitoneal pathology.

It is needless to say that the general and surgical treatment should be different for extra- and intraperitoneal conditions and that failure to appreciate this fact may result disastrously for the patient. It does, however, seem worth while to stress the difficulty of determining in some instances the relationship of a pelvic lesion to the peritoneal cavity, and that because of this difficulty mistakes in diagnosis can easily be made.

Abscesses are the extraperitoneal pelvic lesions that most frequently call for surgical interference. They usually develop as a result of a parametrial infection. Mauriceau, in about the middle of the eighteenth century, described inflammation of the pelvic connective tissue, but it was Virchow who first used the term parametritis to denote inflammation occurring in the pelvis outside of the peritoneum.

Parametritis includes exudates in the pre- and retrocervical tissues, but it is the intraligamentous infiltrations in the base of the broad ligament which are most commonly seen, and which, when suppuration occurs, form the broad ligament abscesses. It is difficult to accurately determine the incidence of parametrial infection, for in mild cases patients may have a moderate elevation in temperature for only a few days, and examinations show nothing more than slight pelvic tenderness. The mild infections are of limited clinical interest for they usually clear up without any particular treatment, but it is very important to recognize promptly the extraperitoneal pelvic abscesses which develop from the more severe types of parametrial infection.

Since 1900, 53 women with extraperitoneal pelvic abscesses have been treated in the Johns Hopkins Hospital, which means that about once in every eight months we see a patient with this condition. Thirty-four of these 53 cases were on the gynecologic service, 19 on the obstetric. Forty of the women were white, 13 colored. When one considers that the relative number of white and colored patients admitted to the hospital is about three to one, it would seem that extraperitoneal abscesses occur with equal frequency in the two races.

Of the 53 extraperitoneal abscesses, 50 were located in the broad ligaments. The other 3 developed in the connective tissue in front of the cervix, 2 of them pointing in the subcutaneous tissue of the midportion of the lower abdominal wall, the third localizing directly under the bladder. In this series, there were no true instances of extraperitoneal abscesses arising behind the cervix, although in several cases suppuration started in one or both broad ligaments and then extended downward and medially toward the retrocervical tissue. Of the 50 broad ligament abscesses, 25 were on the right side, 21 on the left. In 4 instances the infection was bilateral, suppuration developing in both broad ligaments.

TABLE I. ETIOLOGIC FACTORS IN 53 CASES OF EXTRAPERITONEAL ABSCESS IN WOMEN

18 followed abortions.

In 7 of the 18 the abortions were induced by the patient or abortionist.

In 3 the placenta had been removed manually by the family doctor.

In 2 a curettement had been done at home by the family physician.

In 1 a deep cervical tear had occurred at the hands of the family doctor.

In only 5 was the abortion uncomplicated by other factors.

18 followed normal pregnancies but only 6 of the women were delivered by the hospital staff.

11 followed instrumental or operative deliveries.

In 3 of these 11, forceps had been used in the patient's home by the family doctor.

In 1 a curettement had been done in the patient's home by the family doctor.

In 1 the uterus had been packed by the family doctor because of inversion.

In 1 a forceps delivery was done at the hospital.

In 1 a hysterectomy for placenta previa was performed.

In 1 a craniotomy on a dead child was performed.

In 1 a version and extraction were performed on an eclamptic infected woman.

In 2 cervical cesarean sections were performed on infected women.

1 followed a gynecologic operation for dermoid cyst.

1 followed an infection of the vulva and was probably gonorrheal in origin.

4 cases only gave no history of a recent pregnancy, operation or infection.

A consideration of the etiologic factors in this series of extraperitoneal pelvic abscesses is of interest. One case developed after a gynecologic operation for a dermoid cyst, another followed an infection of a Bartholinian gland in a woman from whom the uterus, both tubes and ovaries had been removed several years previously. This is the only instance of a gonorrheal extraperitoneal pelvic abscess of which we have any record in the hospital. A definite history of a recent abortion or pregnancy was obtained in 47 of the 53 cases. In 24 of these the pregnancy had been complicated by either an instrumental or operative delivery or had been terminated by the abortionist.

Of the 47 patients with a history of a recent pregnancy or abortion, only 12 had been taken care of by the hospital obstetric service, and in 6 of these, because of obstetric complications, an operative or instrumental delivery had been necessary, even though several of these women were already infected on admission to the hospital. Since 1900, 36,000 women have been delivered by the obstetric service and, as has just been pointed out, only 6 of this group of women developed broad ligament abscess. This gives us an idea as to how seldom this complication follows normal properly conducted deliveries. Table I shows graphically the etiologic factors in this series of cases.

The onset of symptoms after delivery varied from three to fourteen days but many of the hospital records of the earlier cases do not give exact information on this point. Every one of the 53 women in this series complained of lower abdominal pain, and about half of them gave a history of chills. Gastrointestinal symptoms occurred somewhat rarely. In only 9 cases was there a history of vomiting before operation. In many cases the patient had had such profuse uterine bleeding following an abortion or full-term pregnancy that a marked secondary anemia was present. In fact, the average hemoglobin estimation was only 60 per cent, with readings in some cases as low as 28 and 26 per cent.

Nine patients complained of severe pain on walking, and when admitted to the hospital showed a definite limp. In these cases there was limitation of motion of the hip, the patient holding the thigh flexed and adducted. This is due to a spasm of the psoas muscle and may mislead one into thinking that he is dealing with a tuberculous abscess arising in the vertebrae or hip joint. On the other hand, this limitation of motion of the thigh may help the surgeon to recognize that a pelvic lesion is outside of the peritoneal cavity.

Most of the patients appeared quite ill on admission. The average temperature was 103° and in many cases readings of 105° were recorded. In only a few instances did it fail to reach 101°. The pulse rate corresponded with what would be expected with the elevation of temperature. The leucocytes ranged from 9,000 to 45,000, with most of the patients having a white count of 20,000. Usually the leucocyte count was highest when the temperature was high, as exemplified by a case in which the temperature was 105° and the white count 45,000. Occasionally, however, there were exceptions to this rule, as shown by one of our patients who had a temperature of only 100° and a white count of 26,000. Incidentally this woman was very ill although eventually she recovered.

Tenderness was elicited in every case on palpation of the lower abdomen. An abdominal mass was found in 41 of the 53 cases. In all except the three cases of precervical infection these masses were situated in one or both quadrants of the abdomen just above Poupart's ligament. The size of the mass varied considerably; in some instances merely an indefinite induration was felt, while in others a stony hard tumor extended upward from the inguinal ligament to the level of the umbilicus. The sixth was the earliest day after delivery on which one of these extraperitoneal masses was felt on abdominal examination.

On vaginal examination, in 27 cases definite masses were found in the base of the broad ligaments. In nine others some pelvic induration was made out. Nine patients showed only moderate tenderness, while in three the pelvic examination was recorded as being entirely normal. In these three latter cases, the extraperitoneal pelvic conditions were diagnosed entirely on the history and abdominal examination.

In cases with a characteristic history and typical physical findings, the diagnosis of extraperitoneal pelvic abscess is comparatively easy so long as one bears constantly in mind the thought that some of the pelvic infections in women are extraperitoneal. For instance, there is no excuse for missing the diagnosis in a woman who gives a history of an induced abortion with the later occurrence of chills, fever, and pains in the lower abdomen and on whom abdominal palpation reveals a tender mass just above Poupart's ligament, while pelvic examination shows induration high in the vagina.

However, in some of the patients with extraperitoneal pelvic infections most of the symptoms and signs that we associate with this condi-

tion are lacking, and mistakes in diagnosis can easily be made. For instance, in this series of 53 extraperitoneal pelvic abscesses, 6 were incorrectly diagnosed and as a consequence the treatment the patients received is open to criticism. When one considers that some of the earlier cases occurred in the hospital twenty-five or thirty years ago and that this report is based on the work of 14 different gynecologists and 6 obstetricians, we feel that there is little cause to apologize for our statistics, and yet in order to stress the importance of correctly diagnosing extraperitoneal pelvic lesions we are emphasizing not the 47 cases correctly diagnosed, but the 6 in which the extraperitoneal character of the infection was not recognized.

In 2 of the 6 cases incorrectly diagnosed, the patients did have some mild salpingitis, but the main pathology was extraperitoneal, and the surgeon would have exercised better judgment if he had stayed out of the peritoneal cavity. In the other 4, the peritoneum, uterus, tubes, and ovaries appeared perfectly normal when the abdomen was opened, although large extraperitoneal broad ligament abscesses were present. While we regret these mistakes in diagnosis, these last 4 cases gave us the opportunity of definitely proving that inflammation of the pelvic connective tissue is not always accompanied by inflammation of the pelvic peritoneum, as has been stated by some of those who have written on this subject.

Fifty-one of the 53 patients who had extraperitoneal abscesses were operated upon, and upon leaving the hospital were free from symptoms, the abscess having been evacuated. In 12 cases nonoperative treatment was tried even though the diagnosis of an abscess had been made. Rest, douches, and repeated transfusions were prescribed, but 10 of these 12 finally came to operation. Two patients did leave the hospital without operation, but although the temperature was normal on discharge, abdominal masses were still palpable above Poupart's ligament, and vaginal examination showed induration at the base of the broad ligaments. These two patients were under our care in 1920 and 1922, and although a special effort has recently been made to locate them, the attempt has been unsuccessful, so we do not know how they have fared. Probably they had further trouble.

Not one of the 51 women treated surgically died, although many of them were very ill when operated upon. When discharged, they were symptom-free, and on most of them the abdominal and pelvic examinations were essentially negative. In view of this, we feel that extraperitoneal drainage is the procedure of choice in all cases of extraperitoneal pelvic abscess, even though these two patients did leave the hospital without operation and with normal temperatures.

Because of mistakes in diagnosis, the peritoneal cavity was opened in 6 cases. These mistakes have been noted before, but we are mentioning them again in order to discuss the operative procedure carried out after the surgeon had opened the peritoneal cavity. In four instances the operator incised the peritoneum covering the broad ligament abscess and drained the extraperitoneal condition through the peritoneum. These patients were very ill after operation, but finally recovered. In the other 2 cases the surgeon closed the peritoneum without drainage, made an inguinal incision down to the broad ligament abscess, and drained the condition

extraperitoneally. These 2 patients had a rapid and uncomplicated convalescence. In our opinion, better surgical judgment was exercised in the handling of these two latter cases.

Most authorities believe that an anterior vaginal incision is indicated in the rare instances in which pus has collected under the bladder, and that the abscesses which develop in the subcutaneous tissue of the mid-portion of the lower abdomen are best treated by a lower midline extraperitoneal incision. However, there is still some difference of opinion as to which is the best method of draining broad ligament abscesses which are the suppurative extraperitoneal lesions most frequently encountered. Some operators attempt to reach them through the vagina, using the following technic: An incision is made posterior to the cervix such as is used in draining an intraperitoneal abscess. The peritoneum must not be opened but pushed gently back with the finger. A blunt artery forceps is then wormed upward and laterally toward the involved broad ligament.

In discussing such an operation, it must first be pointed out that it is beset with several dangers. If the forceps happen to pierce the peritoneum covering the indurated broad ligament, it will emerge into the peritoneal cavity and quite likely infect it with the organisms which up to that time had been walled off in the broad ligament. Moreover, in tunneling the instrument laterally toward the broad ligament there is distinct danger that the operator may injure the ureter or uterine artery, as the instrument must pass very close to these structures.

This method of vaginal drainage was attempted in 7 of the 48 patients with broad ligament abscesses that were treated surgically. In 3 of these, the attempt to reach the pus from below was entirely unsuccessful and an extraperitoneal inguinal incision was later necessary. The 4 other patients recovered after drainage through the vagina, but their postoperative stay in the hospital averaged forty-seven days.

A second method of draining broad ligament abscesses extraperitoneally is by what is sometimes called the inguinal route, as shown in Fig. 1.

T. S. Cullen, in an article published in 1917, so clearly described this operation that I shall quote directly from his paper, "A gridiron incision is made above and parallel to Poupart's ligament and the fascia and muscles are split, as in an appendix operation. As soon as the peritoneum is reached, it is pushed toward the median line but without being opened. The two index fingers then gradually spread the broad ligament until the area of induration is reached." Thirty-seven patients in this series were operated on by this method. They all recovered in an average time of twenty-nine days, or eighteen days less than those patients whose broad ligament abscesses were drained through the vagina.

It is of interest that the different surgeons who have had charge of the patients in this series of cases have not agreed as to how soon sur-

gical intervention should be carried out in cases of broad ligament abscess. Most of them have felt that as soon as the diagnosis is made, inguinal extraperitoneal drainage should be instituted, but a few have delayed operation until the inguinal mass felt upon abdominal palpation had reached considerable size and preferably until it had caused bulging of the overlying skin. This latter group of men have contended that by this delay the pus becomes more accessible and that the danger of opening the peritoneal cavity is lessened.

A study of our records has not borne out these claims, for the ten patients whose operations were delayed after diagnosis was made averaged seven days longer in the hospital postoperatively than those operated upon at once, in addition to the two weeks before operation that they

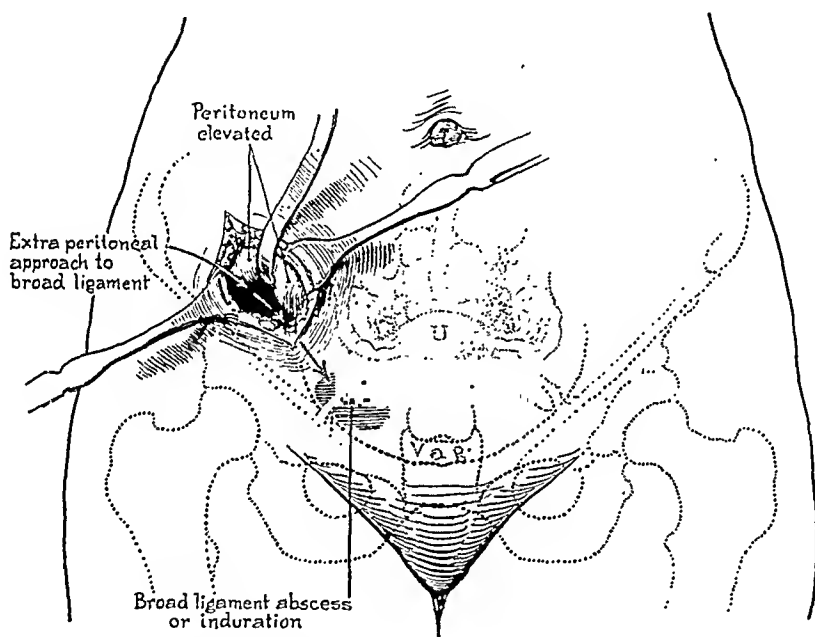


Fig. 1.—The easiest and most satisfactory method of approaching a broad ligament abscess. A gridiron incision is made above and parallel with Poupart's ligament. As soon as the peritoneum is reached, it is pushed toward the median line without being opened (after Cullen).

had spent waiting for the abscesses to become large, making their entire convalescence three weeks longer than that of the patients operated upon promptly. Moreover, the only instance of accidental opening of the peritoneal cavity occurred in one of the ten cases in which inguinal drainage was delayed for two weeks after the diagnosis had been made. Fortunately, no serious consequences followed this operative accident.

Cultures were taken in 33 of the 53 patients on whom operations were performed. Positive growths were obtained in 22 instances; in 11 the cultures were reported to be sterile. The streptococcus was the organism most commonly found, being grown in 11 cases. The staphylococcus came next. It was cultured from five patients. *B. proteus*, the pneumococcus, and a diphtheroid organism were each cultured once.

The colon bacillus was not grown in pure culture from a single case, but it was found three times as a secondary invader, twice along with the streptococcus and once with the staphylococcus. In 8 of the 14 cases in which the streptococcus was the offending organism, the type was not mentioned. Four times it was reported to be the hemolytic variety, once the nonhemolytic, and once it was found to be anaerobic. It has been only in recent years that, largely due to the work of Schottmüller, our attention has been directed to anaerobic organisms in puerperal infections, and special methods have been employed to grow them, so it may well be that they were present in some of the earlier cases of our series in which the cultures were reported as sterile. Incidentally, in 1929, Harris and H. Brown, in their study of 113 cases of streptococic puerperal infections, found the anaerobic with approximately the same frequency as the aerobic variety, and Schwarz and T. K. Brown have in a recent issue of the *American Journal of Obstetrics and Gynecology* stressed the importance of anaerobic streptococci.

The quantity of pus found at operation varied from an ounce to a quart. The speaker had gathered the impression from some of the literature that in broad ligament abscesses the pus is usually thin and watery in character so he was rather surprised to find records of it being thick in eleven cases, foul smelling in eight and yellowish green in seven. In four of the cases from which thick foul smelling pus was evacuated the cultures showed no growth. Fisher and Abernathy have recently stressed that the anaerobic streptococcus can often be found in various putrid and gangrenous lesions throughout the body, and this is of interest to us, for it supports the idea already mentioned that anaerobic organisms were probably present in some of our earlier cases in which the laboratory methods then used failed to show the presence of any bacteria.

There was no operative mortality in this series of cases. As has been said, the patients on whom the broad ligament abscesses were drained by the inguinal route left the hospital in twenty-nine days after operation, while those on whom the inflammatory condition was approached through the vagina had a postoperative convalescence of forty-seven days, or eighteen longer than the first group.

We have recently endeavored to trace all of the 53 patients who had extra-peritoneal abscesses but, frankly, this attempted follow-up has not been very successful. When one considers that it has now been thirty-five years since the first of these women was operated upon and that most of them belonged to the dispensary class of patients who change their residence every few years, this is understandable though disappointing. Still we have in the past few months traced 17 of the 51 patients operated upon, and while this means that we know about the present health of only one out of every three women in this series, a study of the histories obtained from even this small group of patients has brought out interesting facts. Six of the 17 women have had one or more children since leaving the hospital, which seems

to represent about the normal fertility for such a group of women and indicates that extraperitoneal pelvic infections seldom cause sterility. Two women became pregnant within six weeks after leaving the hospital. Apparently it is dangerous for a woman to conceive immediately after she has had a broad ligament infection, for both of the patients who became pregnant so soon after leaving the hospital had uninduced abortions and were readmitted with severe puerperal infections. One of these died from a streptococcal septicemia, and the other recovered only after a long illness. It is of interest that neither of these women on their second admission to the hospital showed any evidence of a localized infection either in the parametrium or pelvic peritoneum. One would suspect that some organism had remained viable in the broad ligament after the patient left the hospital and that they were stimulated to activity by the occurrence of conception so soon after the original infection. These two patients are the only ones that we know of in the entire series whose health after they left the hospital was influenced by a preceding extraperitoneal pelvic infection. Among the group of women who we know have enjoyed good health since their operations are the first two women in this series who were operated upon thirty-five years ago, and who are now both sixty-eight years old.

In summary, this study of extraperitoneal pelvic abscess has brought out these facts:

1. The great majority of cases follow induced abortions or operative deliveries on infected women.

2. A history of lower abdominal pain, chills and excessive bleeding is usually obtained. Few patients complain of gastrointestinal symptoms.

3. Some of the patients complain of pain on walking and hold the thigh flexed and adducted. This finding may be of help to the physician in recognizing that he is dealing with an extraperitoneal pelvic lesion. It is due to spasm of the psoas muscle.

4. In a typical case the temperature and leucocyte count are both high and the examiner can demonstrate abdominal and pelvic tenderness, induration high in the vagina and an abdominal mass just above Poupart's ligament.

5. In many cases the history and physical findings are not typical, and it is easy for the surgeon to mistake a broad ligament abscess for an intraperitoneal condition.

6. All extraperitoneal infections should be drained extraperitoneally.

7. Better results are obtained by draining broad ligament abscesses extraperitoneally through a low McBurney incision (the inguinal route) than by attempting to drain them through the vagina without entering the peritoneal cavity.

8. Extraperitoneal drainage should be instituted as soon as the diagnosis is made. There is no advantage in delaying the operation until the inguinal mass becomes larger.

9. The streptococcus is the organism most frequently cultured from extraperitoneal pelvic infections. Probably in many of the cases in

which the cultures were reported negative, anaerobic streptococci were present, and if special culture methods had been used, positive bacterial growths would have been reported.

10. The pus in many cases of broad ligament abscess is not clear and watery, as might be expected, but thick, yellow and foul smelling.

11. Although many of the patients were desperately ill when operated on, there was no operative mortality in this series of cases. All of the women operated on left the hospital apparently well.

12. Extraperitoneal pelvic infections do not decrease fertility, but there seems to be danger for a woman who has had a broad ligament abscess to become pregnant at once, for in this series the two women who conceived six weeks after leaving the hospital both had puerperal septicemia from which one of them died.

13. Except for the danger associated with conception following immediately after operation, broad ligament abscesses do not apparently affect the health of the patient after the pus has been evacuated and the temperature has returned to normal.

There are in addition to the parametrial abscesses just described other conditions such as myomas and hematomas, which are occasionally seen in the broad ligaments. The treatment of the psoas abscesses due to disease of the spinal column and the pelvic bones belongs to the orthopedic surgeon, but there is a group of psoas abscesses originating in pathologic conditions outside of the bones which may offer diagnostic difficulties to whoever sees them, whether he be orthopedist or gynecologist. These lesions have been discussed by Baer, Bennett and Nachlas in an article on "Non-Spinal Psoas Abscess." As they point out, a suppurative myositis of the posterior abdominal wall, whether it be the result of a metastatic infection or the result of an infected hematoma following trauma, will find in the sheath of the psoas muscle the course of least resistance for the discharge of its pus. Moreover, infections of the kidneys and also those starting in the solid and hollow viscera may cause such abscesses. Then, too, suppurative conditions both tuberculous and nontuberculous sometimes arise in the retroperitoneal lymph glands and the pus may travel along the same path as that taken by a tuberculous abscess arising from one of the vertebrae. Usually these nonspinal psoas abscesses point below Poupart's ligament, while the puerperal broad ligament infections point above it, but despite this fact the two groups of cases may be confused unless the strictest attention is paid to both history and physical examination.

I should like to present brief summaries of four cases taken from my own practice, which demonstrate unusual extraperitoneal pelvic lesions which are of some interest because of their rarity. The first is that of a forty-three-year-old woman who complained of a hard lump in the lower abdomen, which extended in the

midline from the symphysis pubis to within two centimeters of the umbilicus. Since on vaginal examination the abdominal mass could not be differentiated from the uterus, it was thought that we were probably dealing with a myomatous uterus. A lower abdominal midline incision was made and we were surprised to find that the tumor was outside the peritoneal cavity, although lying under the recti muscles. It extended from the region of the bladder to within a few centimeters of the navel as is shown in Fig. 2. The bladder and the recti muscles were not adherent to the

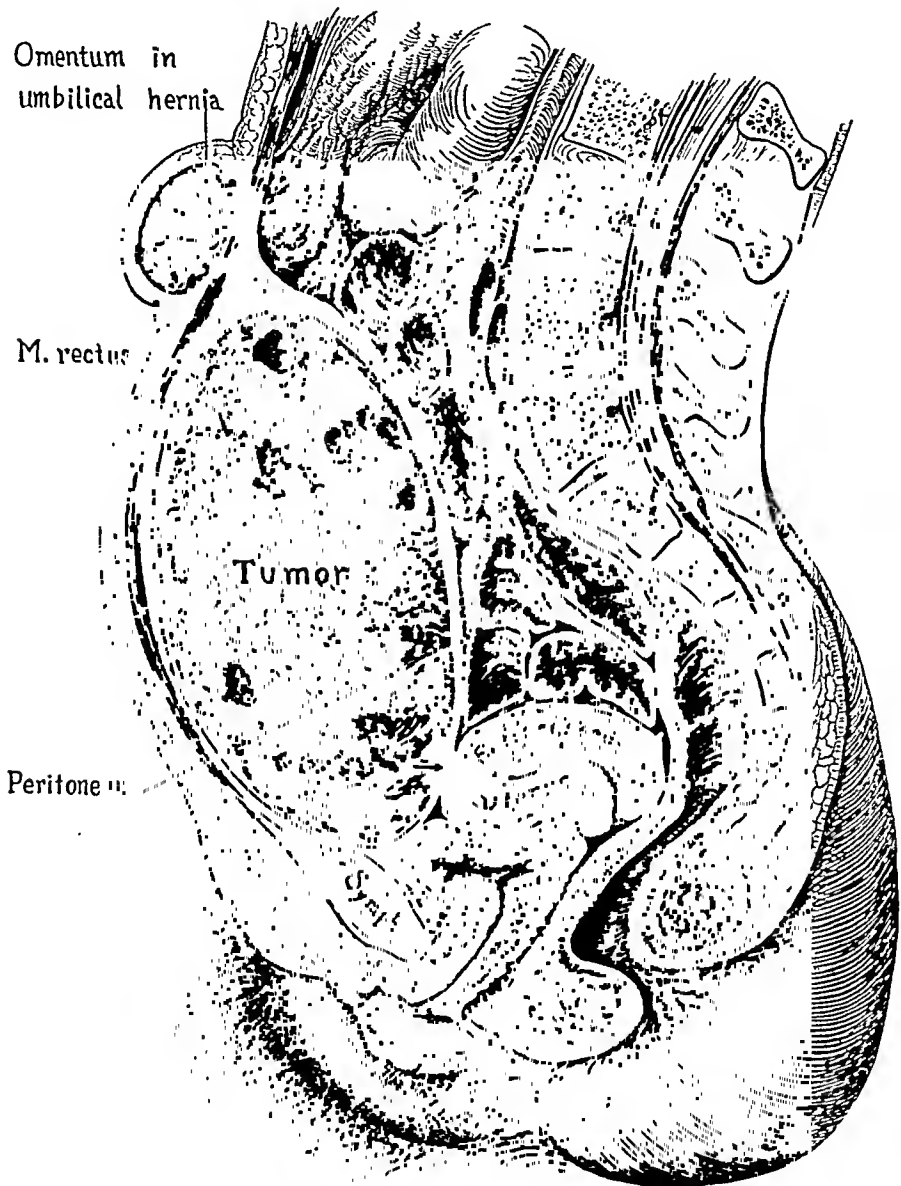


Fig. 2.—Urachal myoma showing its size and position in the properitoneal tissue, between the rectus muscles and the peritoneum.

tumor. It was not necessary to open the peritoneal cavity to remove this growth, but because of a large umbilical hernia, the peritoneum was afterward incised. The uterus contained no fibroids. It was normal in size and appearance as were also the fallopian tubes and the ovaries. The tumor weighed 600 gm., it measured 14 by 10 by 9 cm. There was no pedicle leading from the tumor. The cut surface presented the whorllike appearance of a myomatous growth. Scattered through the firm opaque grayish white tissue were islands of semisolid, spongy, translucent material, such as

is associated with the hyaline degeneration of a myomatous growth. The microscopic sections showed muscle tissue with, in places, considerable hyaline degeneration. There was no evidence of malignancy. A diagnosis of fibromyoma of the urachus was made.

Uraeal cysts and inflammatory conditions arising from the urachus are occasionally met with, as has been emphasized by Dr. Cullen in his book on *The Umbilicus*, but solid tumors of the urachus are truly rare. Up to 1927, when I operated upon this patient, there had been only 20 such cases reported, and 18 of these were malignant. My own and one other case reported by Aveling were the only two uraehal fibroids in this series. It is of interest that Aveling showed his specimen in 1886 before the British Gynecological Society and Bland Sutton wrote a description of its microscopical appearance. Additional cases reported in the past eight years have now brought the total number of benign solid tumors of the urachus up to 7, as was shown in a comprehensive article on this subject by Begg.

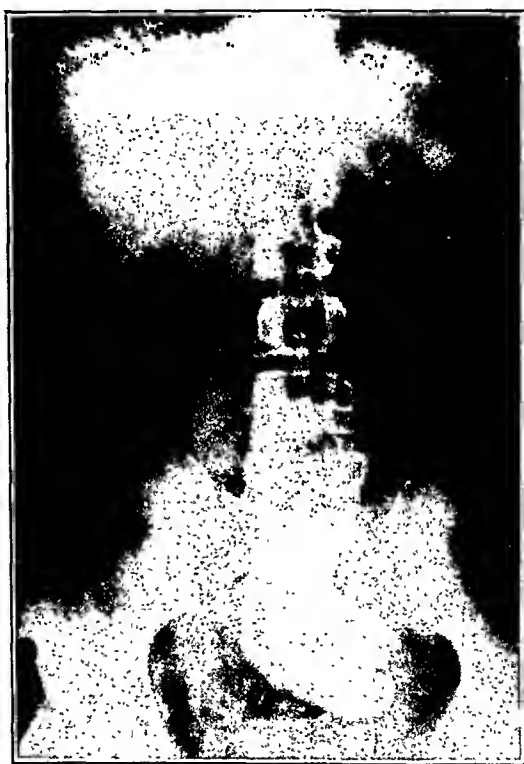


Fig. 3.—Pyelogram showing the pelvic kidney, which has been converted into a large hydronephrotic sac. The kidney lay entirely below the pelvic brim.

Another case is that of a woman who complained of pain in the left side of the lower abdomen. A tender mass was palpable on pelvic examination and as without an anesthetic the left ovary could not be felt separately from this mass, it was our first impression that we were dealing with a cyst or tumor of the left ovary. But because the catheterized specimen of urine showed some pus we decided to cystoscope the patient before operating upon her. Moreover, the consistency and shape of this mass seemed to me to be different from that of any ovarian neoplasm that I had palpated. Fig. 3, a pyelogram, shows that the tumor in the left side of the pelvis was an ectopic kidney, that lay entirely below the pelvic brim. As it was functionless and heavily infected and the other kidney was normal, a nephrectomy was performed. It is important for the following reasons not to mistake a pelvic kidney for a tumor arising in the peritoneal cavity. First, it is usually possible to remove a pelvic kidney without entering the peritoneal cavity. Second, and this is to be

particularly emphasized, if a surgeon unexpectedly should come upon an infected ectopic kidney when he thought he was operating on an ovarian tumor he would hesitate to remove the kidney no matter in what condition he found it, because without having done a differential phthalein test before operation he could not possibly be sure about the function of the other kidney. Unwittingly he might in such a case remove the better of the patient's two kidneys, or in rare cases her only one.

Soon after seeing this last patient, I examined a four-year-old girl, with a tumor the size of a tennis ball. It could be moved freely around the entire lower abdomen and, having in mind ectopic kidneys, I cystoscoped the child. As she was rather uncooperative, this examination had to be done under an anesthetic. By catheterizing the ureters with opaque catheters, placing the child under a fluoro-



Fig. 4.—Mesenteric cyst in a girl four years of age. It measured 10 by 6 by 6 cm. and was roughly kidney-shaped.

scope and then moving the tumor mass without producing any effect on the visualized ureters, we were able to show that this mass did not arise from the kidneys. Then, thinking that the child probably had an ovarian cyst with a long pedicle, we made an abdominal incision. Fig. 4 shows that this cyst arose in the mesentery. Fortunately, it was possible to remove it without injuring the blood supply of the loop of intestine above it, so that an intestinal resection was not necessary.

This, the last case, demonstrates almost as rare a condition as the fibromyoma of the urachus. The patient, a woman thirty-nine years of age, had a moderate sized myomatous uterus but quite separate from the uterus, kidneys and ovaries, all of which structures could be palpated, was an ovoid mass which was deep in the left side of the lower abdomen. This mass could be moved laterally for a few centimeters but no up and down motion was demonstrated. A diagnosis of retroperitoneal tumor

was made, but we could go no further toward determining preoperatively its nature. At operation we first performed a hysteromyomeetomy and then incised the posterior peritoneum. A retroperitoneal cyst lay a little to the left of the midline between the aorta and left ureter and about 3 cm. above the bifurcation of the aorta. In order to rule out an aneurysm, a very small needle was used to aspirate a little of the cyst contents, which to our surprise we found to be milky in character. Without any special difficulty it was found possible to remove this cyst without rupturing it. It measured 10 by 6 by 6 cm. Careful analysis of the cyst contents showed that it contained globules varying in size from 3 to 20 microns, and by using "scarlet red" the presence of large quantities of fat was proved. A diagnosis of retro-



Fig. 5.—A retroperitoneal cyst situated a little to the left of the midline, between the aorta and left ureter and about 3 cm. above the bifurcation of the aorta.

peritoneal chylous cyst was made. Judging from its position, it had probably arisen from the left lumbar lymphatic trunk just before the latter joins the right trunk to form the receptaculum chyli.

In conclusion, I have endeavored, by reporting these unusual conditions, to direct attention to extraperitoneal pelvic lesions and I hope my study of broad ligament abscess has brought out some facts concerning the etiology, diagnosis, and treatment of this condition which may prove of clinical value.

I take this opportunity to thank Dr. Cullen and Dr. Eastman for permitting me to use the records of the Gynecological and Obstetrical Departments in the preparation of this paper.

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DISCUSSION

DR. FREDERICK C. HOLDEN, NEW YORK, N. Y.—Dr. Brady has called our attention to the fact that in the Obstetrical and Gynecological Departments at Johns Hopkins Hospital, there were 53 cases of extraperitoneal abscess opened by the abdominal route, and in none of these cases was there a fatality. Patients die either of peritonitis or blood stream infection and the fact that a broad ligament extraperitoneal abscess developed would indicate either a high resistance of the patient or moderately low virulence of the organism.

Contrary to Dr. Brady's experience, of the large number of extraperitoneal infections at Bellevue Hospital, most of them were localized in the retrocervical space, infiltrating the parametrial tissues of the reetovaginal septum. Most of our cases have, therefore, been best drained by posterior colpotomy. Very rarely was the space between the cervix and the bladder involved. Only a small number also localized between the layers of the broad ligament, becoming accessible for operation by the abdominal route. When such localization did occur, we always drained by the method advocated by Cullen many years ago and described by Brady in this paper.

When does Dr. Brady drain? During the stage of indefinite brawny induration or during the stage of definite mass formation which is stony hard in consistency, or does he wait for fluctuation?

When we first used the Elliott treatment at Bellevue Hospital, the patients selected for treatment were those in which we thought the process would go on to abscess formation and the treatment was instituted to hasten fluctuation, but much to our surprise, resolution took place without abscess formation in a number of these patients.

DR. ARTHUR H. CURTIS, CHICAGO, ILL.—I have become more and more impressed with the relative frequency of adhesions over the anterior surface of the liver in patients who have old gonocoeal lesions of the fallopian tubes and, surprising as it may be, we encounter this type of lesion almost *exclusively* in gonocoeal infections. I refer to cases free from adhesions elsewhere in the upper abdomen. It would seem natural that anterior liver surface adhesions would occur in post-abortive and other infections, but such seems not to be the case.

If we can rule out the more common etiologic factors (such as gonorrheal infection, postabortive and puerperal infection, infections associated with instrumentation, and pelvic tuberculosis), the next most common factor in the causation of chronic pelvic inflammation is the damming back of menstrual fluid and debris by obstructive lesions in the uterus.

In the postabortive and puerperal injection cases I have been greatly impressed with the danger of cervical tears extending into the broad ligament. The only patients I can recall having had a fatal termination after spontaneous full-term labor were three in whom no vaginal examination was made. All three had a spontaneous tear which extended upward into the broad ligament, all developed a blood stream infection, and all died.

DR. N. SPROAT HEANEY, CHICAGO, ILL.—I have long been in favor of draining abscesses of the broad ligaments and of the pelvis, but frequently it is difficult to determine when an abscess is to be drained. If drainage is done too early the patient's illness is accentuated and her convalescence delayed. As long as the patient is having chills, and her temperature is making great excursions each day from normal or slightly above to high and back again, it is too early to drain. When, however, the acuteness of the infection has subsided and instead of long excursions the temperature becomes more constant and yet shows no tendency to disappear, then drainage must be considered. One sign is very helpful, when the minimum temperature each day goes higher so that the base line is steplike, pus is under tension and drainage is indicated.

DR. FRED L. ADAIR, CHICAGO, ILL.—In dealing with extraperitoneal lesions, especially in obstetric cases, we should not forget involvement of the veins of the pelvis and the frequency of thrombophlebitis. In my experience I have found it rather difficult to determine that the process is limited and to exclude involvement of the lymphatic vessels and veins.

In my opinion the approach should be through the most obvious channel, that is, where the abscess is pointing, whether through the vagina or through the abdomen. We sometimes find abscesses which have arisen through extension of the process through the ligaments, and the abscess may be found located very high, even in the perinephritic region.

DR. JOHN A. MCGLINN, PHILADELPHIA, PA.—My experience at the Philadelphia General Hospital is very much like that of Dr. Holden. The infection of the broad ligaments is one of the most common conditions with which we have to deal. At our hospital the usual etiologic factors of postabortal, postpuerperal and gonorrheal infections are the cause in the vast majority of cases; but in the private cases I should say the most common cause of these abscesses is office cauterization of the cervix.

DR. JAMES C. MASSON, ROCHESTER, MINN.—In considering extraperitoneal tumors of the pelvis, one that has not been mentioned, and which in my experience is not uncommon, is extraperitoneal lipoma. I have seen several such tumors, some of them weighing over 30 pounds. The majority of them start in the kidney region, but occasionally they begin in the fatty tissue in the base of the broad ligament. We should keep in mind these tumors, which can be diagnosed generally by careful clinical examinations and tests. They can easily be removed when small, but it is often difficult to do so when they become large, especially if they extend up into the mesentery of the intestine.

DR. WILLIAM R. NICHOLSON, PHILADELPHIA, PA.—My own teachers, Penrose and Baldy, admitted the advisability of opening certain cases above Poupert's ligament, but in actual practice these two men selected few cases which they felt gave the proper indication for this opening. In the majority we waited until the culdesac was definitely involved with swelling and probable fluctuation and opened in that area. I have kept to this practice in my own service.

A supposed pelvic abscess should never be opened without preparation of the abdomen, in order that if a mistake in diagnosis occurs it may be promptly opened.

This I have made an absolute requirement in my service at the Graduate Hospital. I have had two dramatic experiences in which the history, blood examination, and the palpatory findings were those of large pelvic abscesses, and yet on opening the culdesac in both instances we were rewarded, not by pus, but by a tremendous gush of blood. An old, neglected extrauterine pregnancy, resulting in tubal abortion, may give the classical symptoms of pelvic abscess.

DR. BRADY (closing).—In answer to Dr. Holden's question, as to whether or not we wait for fluctuation before operating, I might say that it is our usual procedure to drain extraperitoneally, through the inguinal route, all broad ligament abscesses as soon as a definite mass is palpable above Poupart's ligament. Occasionally no pus is encountered but only a little bloody serum. However, even in these cases the introduction of drains seems to shorten the patient's convalescence.

I agree with Dr. Adair that in broad ligament infections the process is seldom limited to the lymphatics but also involves and extends by the veins. It is of interest in connection with this limitation of some infections to special tissues, to mention again the four cases in which the peritoneal cavity was opened through mistakes in diagnosis. There was no evidence of any peritonitis in any of these cases and still large extraperitoneal broad ligament abscesses were present.

Lipomas of the broad ligament form an interesting group of extraperitoneal conditions, but we have had very little experience with them. In our series we also did not have any instances of perirenal abscess following broad ligament injections, but we did have one patient who developed an ischiorectal abscess two weeks after a broad ligament infection was drained and the same type of streptococcus was cultured from the pus obtained at the two operations.

Of course, the logical way to drain all extraperitoneal abscesses is by the route which leads most directly to the infection, but in our experience, as a general rule, inguinal drainage has yielded us better results than vaginal drainage.

Hunt, Elizabeth: Skin Affections Underlying Pruritus of the Vulva and Anus, Laneet 1: 592, 1936.

In a study of 300 cases of vulval and anal pruritus seven classifications are made and their respective numbers given:

I. <i>General Skin Affections:</i>		V. <i>General Constitutional Diseases:</i>	
Lichen planus	105	Diabetes	12
Seborrheic dermatitis	69	Secondary anemia	2
Psoriasis	17	Disseminated sclerosis	1
Eczema	2	VI. <i>Psychic</i>	8
Leucoderma	4	VII. <i>Various:</i>	
II. <i>Dermatitis Traumatica et Venenata</i>	59	Lichenoid eruption with oral sepsis	2
III. <i>Local Causes:</i>		Lichenoid eruption with cholecystitis	1
Vaginal discharge	3	Lichenoid eruption with malignant neoplasm of liver	1
Vaginal prolapse	2	Senile pruritus	2
Hemorrhoids	2	Imperfect hygiene	2
IV. <i>Parasites:</i>		Undetermined	3
Scabies	2		
Ringworm (Dhobie itch)	1		

The author points out the necessity for an accurate diagnosis to prescribe and treat correctly. Particular attention is given to lichen planus and its differentiation from leucoplakia, for in the latter vulvectomy is indicated. Lichen planus should be diagnosed only when there are similar typical lesions at other sites. Seborrheic dermatitis of the genitalia is almost always associated with the disease elsewhere on the body.

H. CLOSE HESSELTINE.

THE RELATION OF THE ENDOCRINE SYSTEM TO TUMOR GROWTH*

THE EFFECT OF HYPOPHYSECTOMY AND PITUITARY GROWTH HORMONE ON TRANSPLANTABLE RAT SARCOMA

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FOR a number of years attempts have been made to link the endocrine system with carcinogenesis and tumor growth. Most of the early studies dealt with the behavior of tumor tissue implanted in close contact with endocrine tissue. The most noteworthy of these was published by Desider Engel, whose observations covered a wide range of endocrines. Engel pointed out that great variations exist in the affinity of hormones for neoplastic tissue. He also pointed out that age, sex, race, and species modify such relations. In his experiments, thymus and thyroid showed inhibitory qualities, the gonadal group had no effect upon tumor growth, and the pituitary gland suggested the presence of a tumor growth accelerating agent. In some later experiments, others showed the tumor inhibiting action of endocrine tissues to be nonspecific and probably not different from the qualities of various somatic tissues.

This particular line of investigation made little progress until the advent of the isolation of specific hormones. Since then, considerable progress has been made and some extremely interesting informations have been obtained. One of the most interesting of these is Lacassagne's study of the relation of estrogenic hormone to carcinogenesis. Lacassagne observed the occurrence of mammary cancer in male mice after the administration of large doses of estrogenic hormone. In this particular strain of mice the females were afflicted with spontaneous cancer of the breast, but the males were rarely victims of this disease. Although the number of animals studied was small, the results are significant as far as selective experimentation is concerned. However, these results do not yet warrant a general application, because they do not prove that estrogenic hormones as a whole can produce mammary cancer under any conditions and in all mammals. The only deduction permissible is that in the particular strain of mice studied by Lacassagne, the mammary cell of the male possesses a tendency

*Supported in part by grants from the Rockefeller Fluid Research Fund of Stanford University School of Medicine, and from the Scientific Research Committee of the American Medical Association.

toward functional mutation of carcinogenic propensity which is dormant in the male but can be awakened by a specific stimulus, such as an estrogenic hormone not ordinarily present. The mammary cell of the female possesses the same carcinogenic propensity in an active state, and since it is constantly exposed to this estrogenic hormone, malignant degeneration is a common occurrence. This subject was discussed again by Loeb in 1935 on the basis of further laboratory evidence. The basic principle underlying this process must be quite similar to that of malignant degeneration following prolonged chronic irritation. Under ordinary circumstances, chronic irritation does not produce cancer. Various other receptive factors must be present before cell mutation reaches a malignant stage. Above all, the cell exposed to irritation must have the faculty of undergoing more than ordinary mutation; the stimulus necessary to set off this process must be specific; and the host must lack resistance to malignant degeneration. This is very well demonstrated in Fibiger's experiments.

Fibiger produced gastric cancer by feeding rats cockroaches infected with certain nematodes. The development of this gastric cancer involved four factors: a specific nematode (spiroptera) had to be present in a specific cockroach (Cuban); the rat fed had to be of a specific species (Norwegian), and then cancer would occur only in a specific organ (the stomach). Even then, not all of the animals would be infected. As soon as the chain of events was broken the results were largely negative.

The more one studies the behavior of cells, the more one is impressed with potentialities of the individuality differentials of cells, so ably described by Leo Loeb. Cells develop a tendency toward functional mutation in changed environments. In other words, the individuality differentials assume injurious faculties in an inadequate environment. The theory of organ and tissue differentials is too complicated to be expounded here. Suffice it to say that the changes of cell characteristics according to this theory are probably largely extrachromosomal phenomena.

There is comparatively little known about the relation between extrachromosomal influences and the incidence of malignancy. That such a relation exists is certain. We call particular attention to Loeb's studies on cell individuality and transplantation of tissues, and to the studies of Little, and Murray and Little, of the existence of extrachromosomal influences on the incidence of mammary tumors in mice. We are convinced from our own tumor studies, which have been carried on for more than eight years and are not yet published, that malignant degeneration is not as simple a process as can be explained on the basis of the Mendelian Law. We agree with Little, and Murray and Little, that the existence of chromosomal influences is of importance in the genesis of neoplasms but that a simple hereditary mechanism is not the sole explanation. It is only natural that in studying extrachromosomal influences cancer research has turned to the hormones. In our opinion, Lacassagne's experiments typify the relation of hormones to tumor growth on this basis.

The entire question of the relation of the endocrine system to tumor growth is exceedingly complicated. Recently Fischer-Wasels evaluated the important contributions in an impartial way. His attitude toward the numerous published suggestions that any hormone may have a direct influence on the origin or growth of malignant tumors, whether in animal or man, is that of disbelief. Fischer-Wasels has repeatedly pointed out that it is not a sudden extraneous factor which changes the normal

into a malignant cell, but that this mechanism is dependent upon a sequence of circumstances ranging over a long period of time. Cells of different tumor constituencies produce different chemical substances and probably are receptive only to a limited number of chemical reactions in the sense of Loeb's theory of cell individuality and characteristics. Probably the same is true of hormonal reactions. Since Otto Warburg demonstrated that the metabolism of the malignant cell differs considerably from that of the normal, it has been suggested that hormones may play a part in bringing about this change in normal cells, with the ultimate result of malignant degeneration. The obvious objection to such speculation is the lack of accurate information concerning the chemical and physiologic individuality of both the normal and the malignant cell.

EXPERIMENTAL STUDIES

Since we have studied tumor growth on the basis of developmental occurrences over a period of years, we could not escape delving into the secrets of the hormonal apparatus. As previously recorded (Emge), we have witnessed the change of transplantable mammary adenofibromas into fibromas and ultimately into sarcomas of a very vicious type. We believe that this alteration has followed the intensification of individuality factors resulting from changes in the biologic surroundings of transplanted tumor materials. In the course of transplantation over many generations, the tumor tissue has been passed through old and young, males and females, castrates of both sexes, and ultimately into highly inbred animals. The result has been sarcoma. At the same time, we have been able to prevent these mutational changes if no new factors were introduced. Thus we still have the original adenofibroma tumor strain and also the fibroma strains developed from it. We have not been able to obtain carcinoma, at least not transplantable carcinoma, by our method, although microscopically a malignant degeneration of the parenchyma is evident in such tumors, which, when again transplanted, produce rapidly growing but cytologically benign adenofibromas that recur after removal but do not metastasize. We are searching for an explanation, and among other studies we have followed the lead of other investigators in studying the relation of the hypophysis to tumor growth.

One of the reasons for the assumption that the hypophysis may bear a relation to tumor growth is based on the finding of cellular changes in the eosinophilic apparatus when tumor growth is present elsewhere in the body.

Such changes were described by Guyer and Claus in rats bearing Flexner-Jobling carcinoma. They were also seen by Wyeth in the hypophyses of carcinoma patients. The reaction expresses itself in vacuolation of the eosinophilic components, similar to castration reactions. But McEuen, Selye, and Thomson hold that this reaction is not specific since it can be produced by other tissues, provided decomposition occurs after implantation. These investigators therefore concluded that the pituitary response ascribed by others to the presence of tumor growth represents only a reaction to chronic absorption of toxic materials.

Another reason for linking the hypophysis with tumor growth is the finding of large amounts of gonadotropic hormone in the urine of certain cancer victims.

This problem was first investigated by Zondek, Zondek and Hartoch, who studied the effect of gonadotropic hormone on the growth of Ehrlich's mouse carcinoma. After failing to influence the growth rate of this carcinoma through the administration of various hormones derived from the thyroid, adrenal, and gonads, these investigators resorted to the administration of large doses of gonadotropic hormone. Various degrees of inhibition and retardation of this neoplasm occurred, but cytologic studies failed to prove that this therapy actually destroyed cancer tissue. It may be concluded, therefore, that while gonadotropic hormone may exert an inhibiting influence on the growth of certain tumors, it does not possess carcinocidal faculties. Cannova repeated these experiments with smaller dosages of the same hormone and obtained similar, but less striking, results. Therefore, it is likely that the tumor growth-retarding action of the gonadotropic hormone is quantitative in nature.

In some of our unpublished studies of the action of gonadotropic anterior pituitary-like and estrogenic hormones on the growth rate of benign tumors in young rats, we have observed that when the dosage of this hormone is increased sufficiently to disturb the normal state of health, tumor growth is retarded in a way similar to that caused by chronic disease, starvation, or cachexia. Consequently we have serious doubt that the action of any hormone as a general tumor-inhibiting agent is specific in a broad sense.

This is borne out to some degree by Saphir's studies on the increase of gonadotropic hormone in the urine of patients afflicted with genital and extragenital malignancies. It was only in the genital that Saphir found striking increases of gonadotropic hormone. The gonadotropic reaction observed by Zondek and others, therefore, may have to be interpreted as being specific only for tumors of genital origin. This reaction probably represents an intensification of pituitary response to an increased output of gonadal hormone when the mass of certain cells of genital origin is markedly increased. It is therefore of considerable interest that Paul Engel and Tanzer, who repeated the experiments of Zondek and others with different tumors such as various transplantable mouse sarcomas, found that the growth of these tumors either could not be, or was only slightly, retarded. Recently Ludwig and v. Ries thought the mice of their colony were refractory to the inoculation of an unspecified cancer emulsion when previously treated with prolactin. All of these observations are very interesting and important, but they demand broader applications in tumor experimentation before they can be accepted as facts applicable to the principles of tumor growth in general.

A third reason for linking the pituitary gland with tumor growth is based on the supposition that the growth hormone may play an important part in tumor development. The study of this problem presents considerable technical difficulty because it requires the destruction of the hypophysis, with a resultant high mortality of experimental animals. It also introduces various new factors which are not present under normal conditions, as exemplified by the marked depression of metabolism in general and the complete alteration of hormonal rela-

tions. The other endocrine glands very rapidly undergo atrophy after pituitary ablation. Hence, hypophysectomy eliminates not only pituitary factors but it also decreases other endocrine secretions which may bear directly on the physiology of certain neoplasms.

The effect of hypophysectomy on tumor growth has been studied by Hayashi, Bischoff and others, McEuen and others, Ball and Samuels, and Franseen and McTiernan. With the exception of Hayashi, who studied rabbit sarcoma, these investigators used either Walker rat carcinoma 256, rat sarcoma R-10, or mouse sarcoma 180. Bischoff, Maxwell, and Ullmann also studied spontaneous mouse mammary carcinoma. Hypophysectomy in mice is very difficult and the results are rather discouraging. The investigators last mentioned therefore resorted to heavy irradiation to the pituitary region either by x-ray or by radon-seed implantation, using the decrease of body weight as the standard for the effectiveness of this method.

We shall not enter into the controversy as to the efficacy of destroying pituitary function by irradiation versus hypophysectomy, but shall content ourselves with a brief review of the end-results reported by the various groups of workers. It may be stated in a general way that all investigators agree that hypophysectomy in rats or the destruction of pituitary function by irradiation in mice leads to a retardation of tumor growth similar to that seen in prolonged starvation, but to a slightly greater degree. There are differences in response in different types of tumors.

McEuen and Thomson contend that the retardation of growth in hypophysectomized animals is probably independent of the pituitary growth hormone but constitutes a part of a general decrease in somatic response after hypophysectomy. These workers believe that their studies tend to discount the importance of the anterior pituitary hormone, particularly the growth hormone, in tumor growth. This opinion is not shared by Ball and Samuels, nor by Bischoff and his coworkers. Franseen and McTiernan very recently reported experiments in which hypophysectomy showed little or no retarding influence in Walker carcinoma 256.

In the following paragraphs we submit the results of our own observations on the relation of the growth hormone to the growth of the autogenous mammary rat sarcoma developed by us and designated hereafter as rat sarcoma E (Emge), the particular strain being designated by numbers. The cellular composition of these strains varies from a highly mature spindle-cell sarcoma to a fairly immature mixed-cell type. In the following experiments, strains E-2 and E-5 were studied. Both strains produce rapidly growing tumors which ordinarily kill in from three to four weeks if not removed. They do not metastasize, but recur rapidly after removal. Transplantation yields 100 per cent "takes." The growth rate of these tumors is uniform and conforms to the basic laws of tissue growth, always showing a slight retardation in the volume curves with increasing size, as described by us in our studies of tumor growth in pregnancy (Emge).

The growth rate in comparison with that of the body of the host is positively heterogonic,* i.e., the tumor growth rate far exceeds that of the body of the host. Since the tumor does not metastasize and grows well in the groin of the host, observations and measurements can be made with reasonable accuracy. The strain of rats studied is a Wistar Institute derivative, bred pure at our institution for some thirty years.

Each experiment was started with a much larger number of hypophysectomized rats than shown in the accompanying charts. The very high mortality reduced the number of completed observations to a few. For the sake of uniformity we preferred to eliminate incomplete observations and report only on tumors which grew for a sufficiently long period. The total number of animals studied is 74. This number is rather small, and requires a continuation of the study before final conclusions can be offered.

In order to save space, all observations are recorded in graphic form. Body weights are charted in the conventional way. Tumor volumes, estimated according to the prolate-spheroid formula ($4/3\pi ab^2$), are recorded on logarithmic paper, and the curves therefore appear steeper than when charted in the conventional manner.

EXPERIMENT 1

Donor L-1021, female, Sarcoma E-2, 13 animals (Fig. 1). Ten of the animals studied were approximately seventy-three days of age and 3 were one hundred and forty days old at the time of tumor implantation. As indicated in the charts, the majority of the animals were males. In the hypophysectomized group, animal "A" was found to have been only partially hypophysectomized. Groups 2 and 4 were injected with 1 c.c. of a growth hormone prepared by us according to the Evans formula. Injections were given subcutaneously, beginning with the day of implantation and continuing daily for the duration of the experiment. This growth hormone was not standardized and therefore the actual amount given was not known except for quantity. However, it was found to be very active. It probably contained traces of gonadotropic hormone, since we found macroscopic changes in the ovaries. All animals were hypophysectomized at the time of implantation.

A comparison of the body weight curves of the four groups (see Chart 1) shows that the body weight of the hypophysectomized animals failed to rise at the rate observed in Groups 1 and 2. The partially hypophysectomized animal "A" in Group 3 showed a mild rise, but considerably below the expected increase for the normal. The older animals "A" in both Groups 1 and 2 did not show the marked rise in body weight that occurred in the younger animals. The behavior of the body weight of animal "B" in Group 4 is unusual and probably signifies a greater receptiveness to the administration of the hormone. Comparing Groups 1 and 2, it is evident that the majority of the animals given hormone gained more rapidly

*Julian Huxley, in *Problems in Relative Growth*, styles an organ growing at the same rate as the body, as *isogonic*, and at a different rate as *heterogonic*, as originally suggested by Pézard in 1918. *Positively heterogonic* means an increase in relative size as related to growth. *Negatively heterogonic* means a decrease in relative size but an increase in absolute size.

than the controls, and a comparison of these two groups with Group 3 shows that hypophysectomy distinctly interfered with an increase in body weight. The response in Group 4 was controversial and inconclusive.

On Chart 2 are the logarithmic growth curves of tumor volumes recorded as successive prolate-spheroids. A comparison of the four groups shows only minor

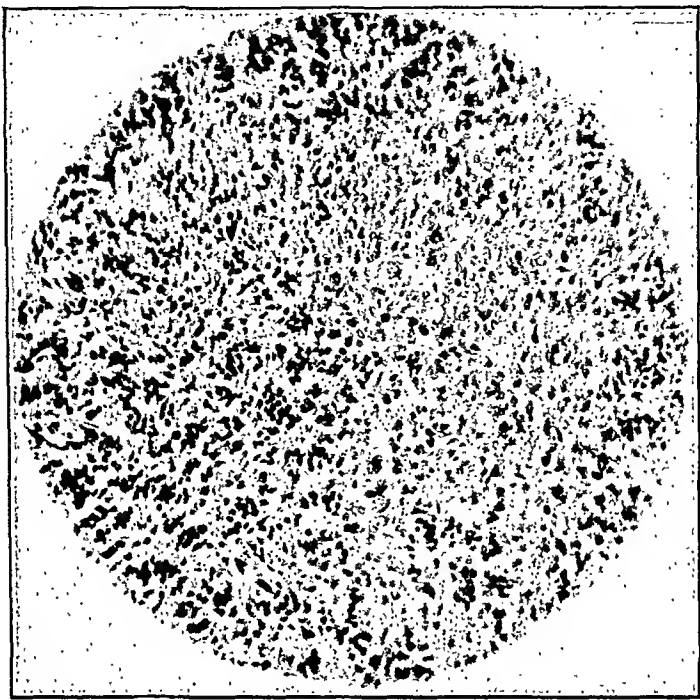


Fig. 1.—Experiment 1. Donor L-1021, female, Sarcoma E-2.

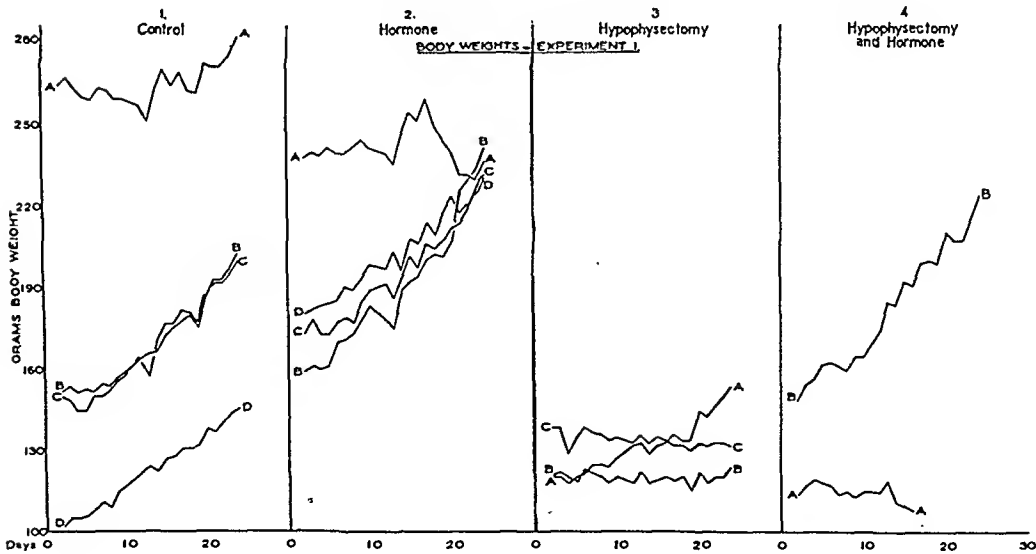


Chart 1.—Experiment 1. Body weight chart. Donor L-1021 ♀, Sarcoma E-2. Animal age: 10 animals approximately 73 days, 3 animals 140 days. Sex: Males (♂) and females (♀) as indicated in tumor volume chart. Hypophysectomy: At time of implantation. Total ablation of pituitary in all except A of Group 3. Hormone: 1 c.c. Evans' alkaline extract subcutaneously daily from time of tumor implantation. Days: Time from tumor implantation to removal.

differences between the ultimate volumes reached. There is a greater variability with a slight increase in tumor volume in Group 2 and a slight decrease in Group 3. In

Group 4, animal "A" died prior to the ultimate time for observation, but judging from the volume reached by the time of death, this tumor probably would have been equal in volume to "B." In general, the differences in ultimate volume between the four groups are not great, and when compared with the body weight curves it is apparent that there is a similar, but more marked, variation. In Group 2, animal "A" showed the same drop in body weight as it showed in tumor volume. In Group 3, animal "A," which was only partially hypophysectomized, showed also a greater body weight and tumor volume than "B" and "C." In Group 4, the marked increase in body weight is not explainable on the basis of unusual increase in tumor volume, since this tumor did not reach an unusual size as compared with controls.

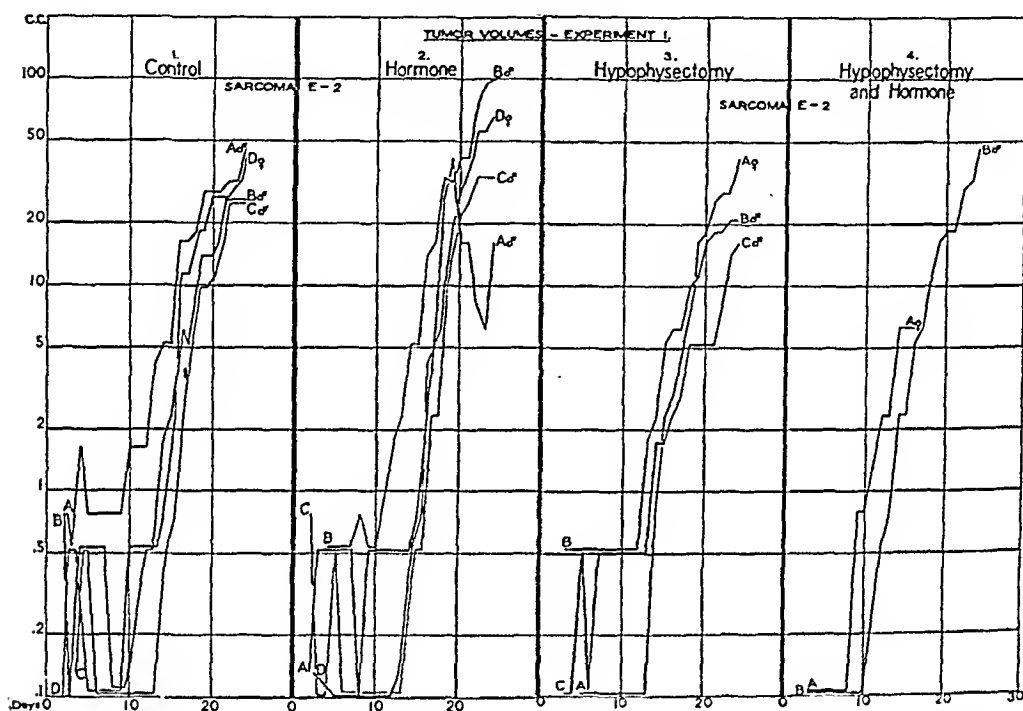


Chart 2.—Experiment 1. Tumor volume chart. Donor L-1021 ♀, Sarcoma E-2. c.c. Tumor volume (according to prolate-spheroid formula). Days: Time from tumor implantation to removal. (See body weight chart of Experiment 1.)

EXPERIMENT 2

Donor L-1111, male, Sarcoma E-5, 20 animals (Fig. 2). Sixty-day-old male animals were studied. Hypophysectomy and tumor implantation were carried out at the same time. The growth hormone used in Experiments 2, 3, and 4 was Antuitrin-Growth, prepared and standardized by Parke, Davis and Company. In this experiment, 0.5 c.e. (5 R.U.) of growth hormone was injected intraperitoneally daily, beginning three days after tumor implantation. All recordings on Charts 3 and 4 were made according to the methods described in Experiment 1.

The behavior of the body weight curves, with the exception of Group 2, is quite similar to that of Experiment 1. There are certain variations, such as animal "C" of Group 1, which showed an unusual increase in body weight, probably due to the rapid growth of the tumor (see Chart 3). The similarity in body weight gain of Groups 1 and 2 is evident. The behavior of the body weight curves of the animals of Groups 3 and 4 conforms to that expected in hypophysectomized animals with or without replacement therapy. A comparison of the volume curves, on the other hand, shows again that variations occur in each group. In the control group, tumor volume showed a greater variation than expected, probably due to extensive abscess

formation and surface erosion of the tumor in animal "A," and to some degree in animal "D." In the hypophysectomized group, tumor volume was generally below that of Groups 1 and 2, but the decrease did not parallel the marked decrease in

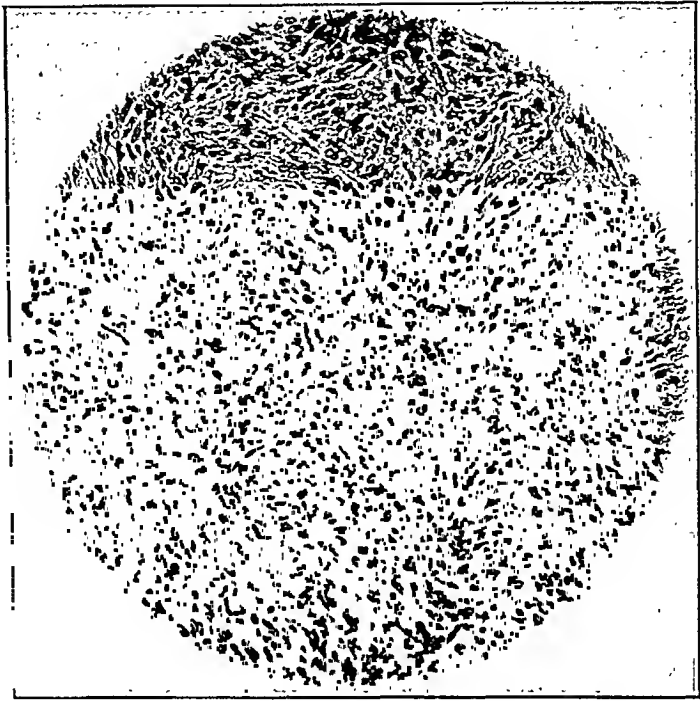


Fig. 2.—Experiment 2. Donor L-1111, male, Sarcoma E-5.

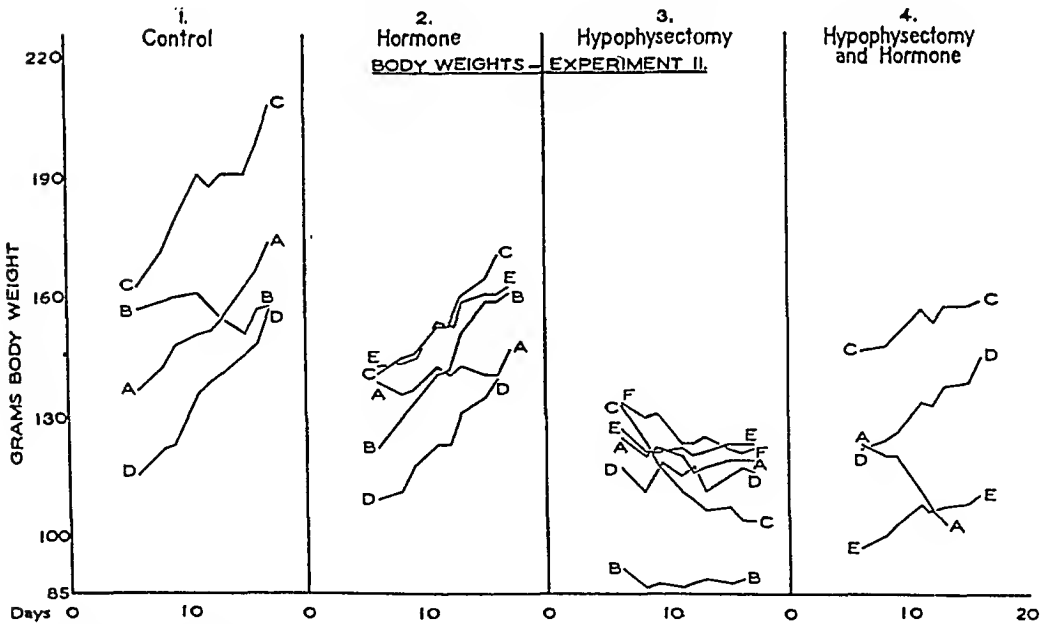


Chart 3.—Experiment 2. Body weight chart. Donor L-1111 ♂, Sarcoma E-5. Animal age: 60 days. Sex: Males. Hypophysectomy: At time of tumor implantation. All animals completely hypophysectomized. Hormone: Antuitrin growth (Parke, Davis & Co.). 0.5 c.c. (5 R.U.) intraperitoneally daily beginning three days after tumor implantation. Days: Time from tumor implantation to removal.

body weight. The small dose of hormone given in Group 4 was sufficiently potent to allow the animals a constant but retarded weight gain, except animal "A," which was unaffected.

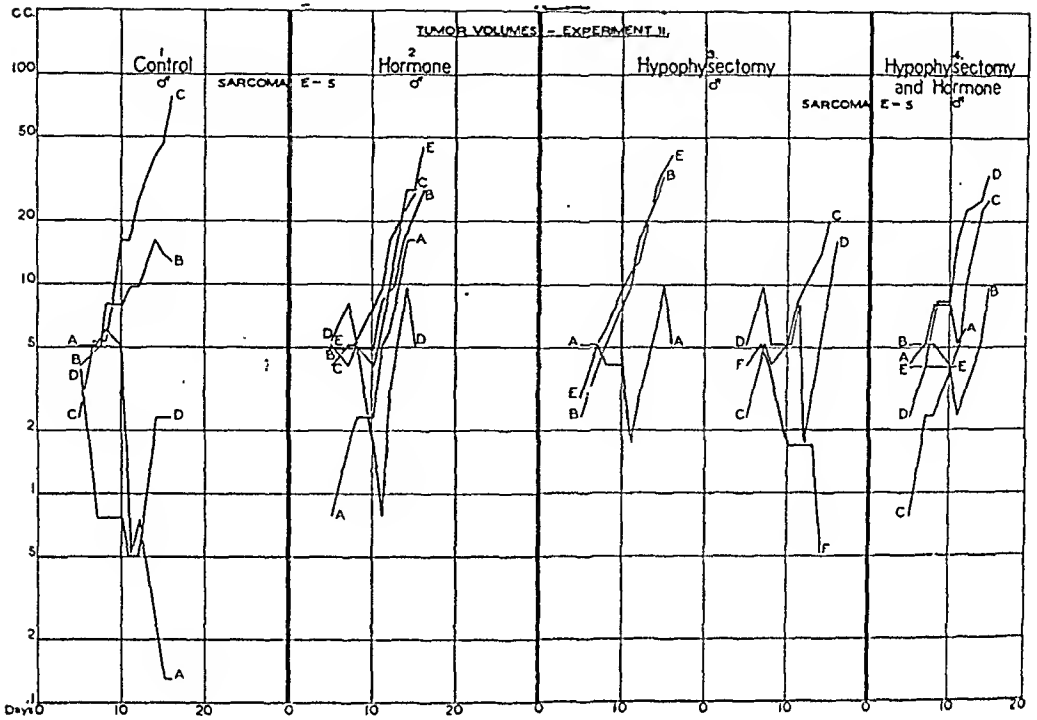


Chart 4.—Experiment 2. Tumor volume chart. Donor L-1111 ♂, Sarcoma E-5. c.c. Tumor volume (according to prolate-spheroid formula). Days: Time from tumor implantation to removal. (See body weight chart of Experiment 2.)

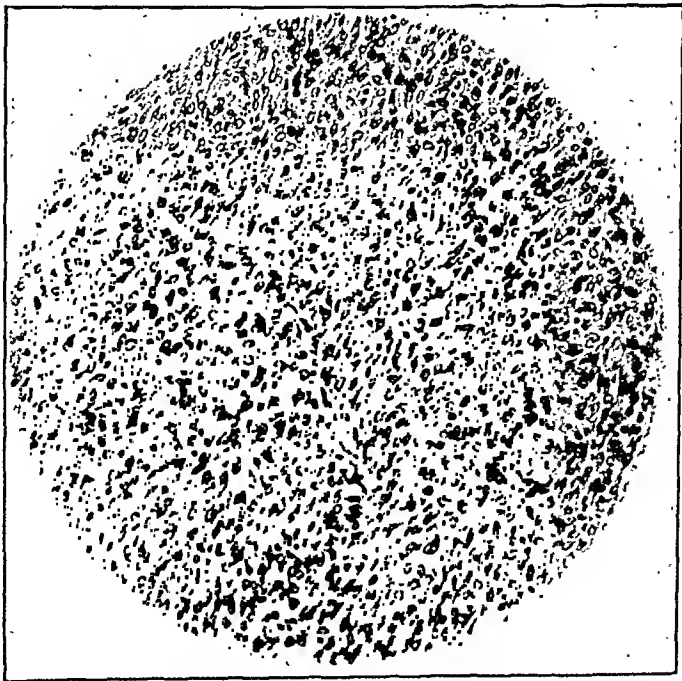


Fig. 3.—Experiment 3. Donor L-1164, male, Sarcoma E-5.

EXPERIMENT 3

Donor L-1164, male, Sarcoma E-5, 18 animals (Fig. 3). All animals studied were males fifty-seven to sixty-one days old. Hypophysectomy was done from one to three days after implantation of the tumor. In Groups 2 and 4, 1 c.c. (10 R.U.) of growth

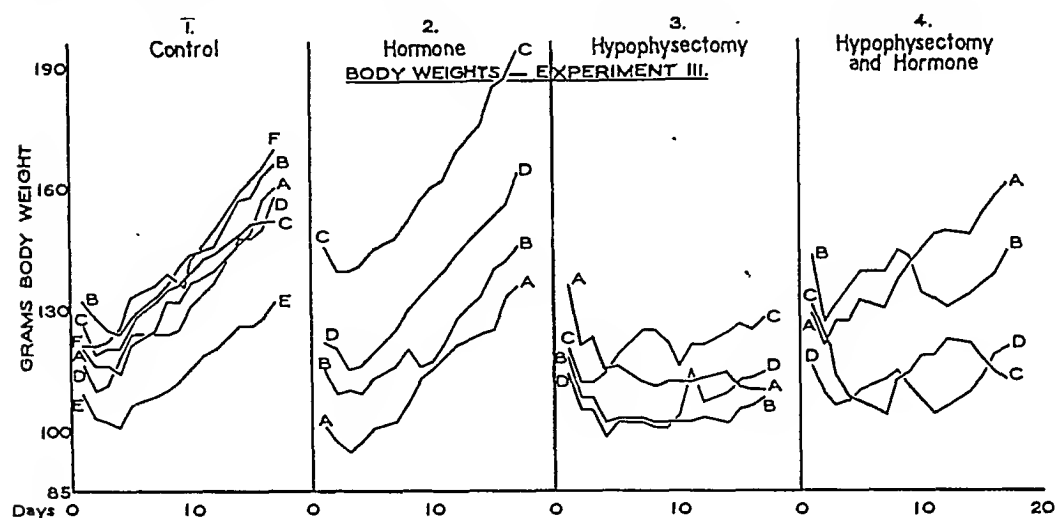


Chart 5.—Experiment 3. Body weight chart. Donor L-1164 ♂, Sarcoma E-5. Animal age: 57 to 61 days. Sex: Males. Hypophysectomy: One to three days after tumor implantation. All animals were completely hypophysectomized. Hormone: Antuitrin growth (Parke, Davis & Co.). 1 c.c. (10 R.U.) intraperitoneally daily from time of tumor implantation. Days: Time from tumor implantation to removal.

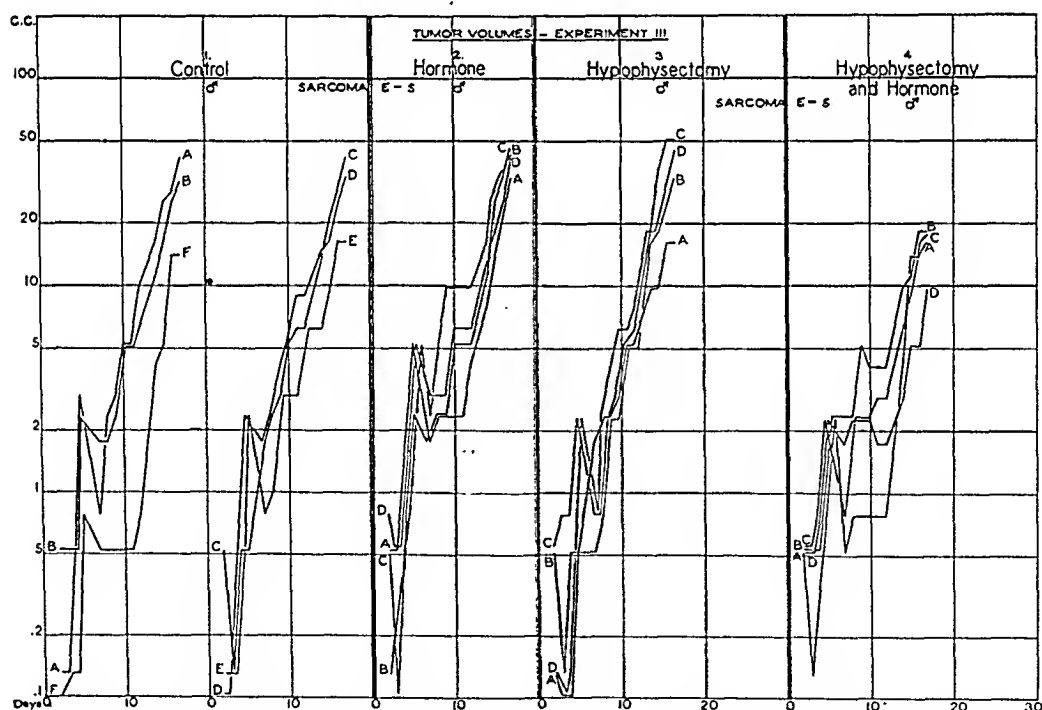


Chart 6.—Experiment 3. Tumor volume chart. Donor L-1164 ♂, Sarcoma E-5. c.c. Tumor volume (according to prolate-spheroid formula). Days: Time from tumor implantation to removal. (See body weight chart of Experiment 3.)

hormone was injected intraperitoneally daily from the time of implantation. A comparison of the body weight curves on Chart 5 shows the general differences discussed in the previous experiments. The response of the hypophysectomized animals to the hormone is again evident. A comparative study of the tumor volume

curves on Chart 6 shows less difference between Groups 1, 2, and 3 than in the previous experiments. There also is a greater uniformity of tumor volume in general. It is apparent that the nonhypophysectomized animals receiving growth hormone did not grow larger tumors than the controls. Tumor volume in the hypophysectomized animals was about as great as in Groups 1 and 2, while in Group 4 it was definitely below that of the other three groups. The behavior of the tumor in Group 4 was unusual, particularly since the body weight curves of the hosts increased as expected. Therefore, the tumor growth is negatively heterogonic; i.e., the volume curve of the tumor is below that of the control when tumor volume and body weight are compared.

EXPERIMENT 4

Donor 32614, male, Sarcoma E-2, 24 animals (Fig. 4). All animals studied were males sixty-one to sixty-eight days old. Of the original 25 animals hypophysectomized, 7 lived long enough to be included in this experiment. In both Groups 3

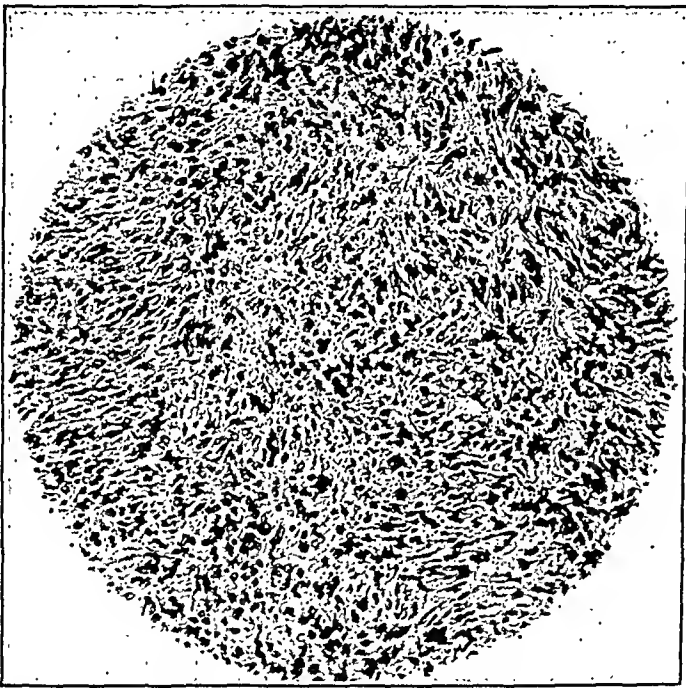


Fig. 4.—Experiment 4. Donor 32614, male, Sarcoma E-2.

and 4, partial hypophysectomies occurred. Implantation of tumor tissue was postponed for two weeks after hypophysectomy. All animals were implanted on the same day. A group of the controls, as well as of the hypophysectomized, were given daily intraperitoneal injections of 2 c.c. (20 R.U.) of growth hormone. Injections were begun on the day of implantation. The high mortality among the hypophysectomized animals, and particularly among those receiving hormone, precluded our obtaining sufficiently long observations to be recorded here. All animals, with one exception, were sacrificed 14 days after implantation. Chart 7 graphically demonstrates the increase in body weight and definitely shows that the rate of weight increase in Groups 1 and 2 is about equal. Growth hormone failed to increase body weight. In the hypophysectomized group, it was demonstrated that complete hypophysectomy prevented weight increase. The presence of a very small fragment of pituitary gland, on the other hand, as demonstrated in animal "D" of this group, permitted a normal weight increase for three weeks, when a slight loss of weight was noted. The same may be seen in Group 4, in which hypophysectomized animals received hormone. The partially hypophysectomized animals "A" and "C" increased

in weight normally. The one animal which was completely hypophysectomized continued to lose weight in spite of the fairly large dose of growth hormone administered. It may be seen in all groups that the implantation of the tumor interfered very little with the expected weight behavior. The continued drop in weight of

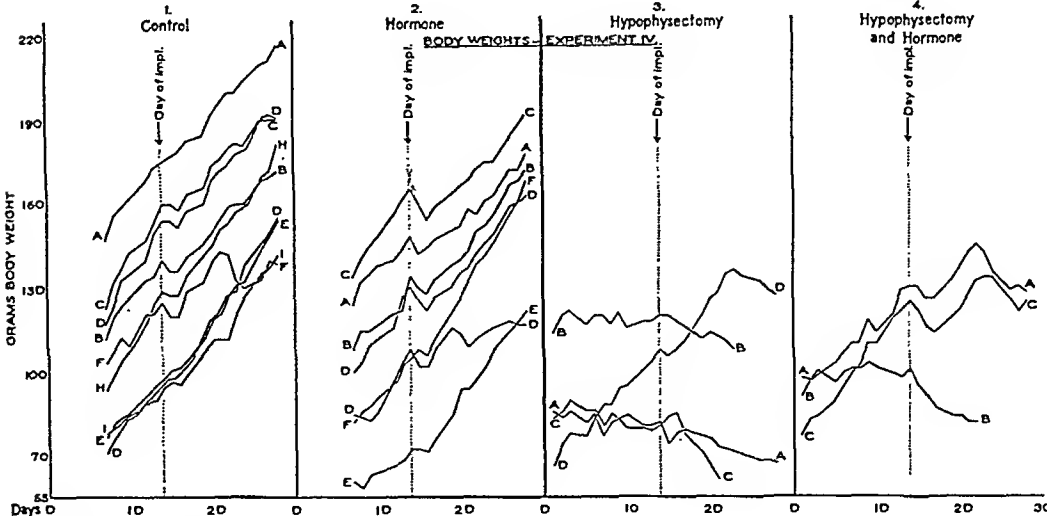


Chart 7.—Experiment 4. Body weight chart. Donor 32614 ♂, Sarcoma E-2. Animal age: 61 to 68 days. Sex: Males. Hypophysectomy: Two weeks prior to implantation. In Group 3, Animal D and in Group 4, Animals A and C are partially hypophysectomized. Hormone: Antuitrin growth (Parke, Davis & Co.). 2 c.c. (20 R.U.) intraperitoneally daily from time of tumor implantation. Days: Time from observation (approximately two weeks before tumor implantation) to tumor removal. Day of implantation indicated.

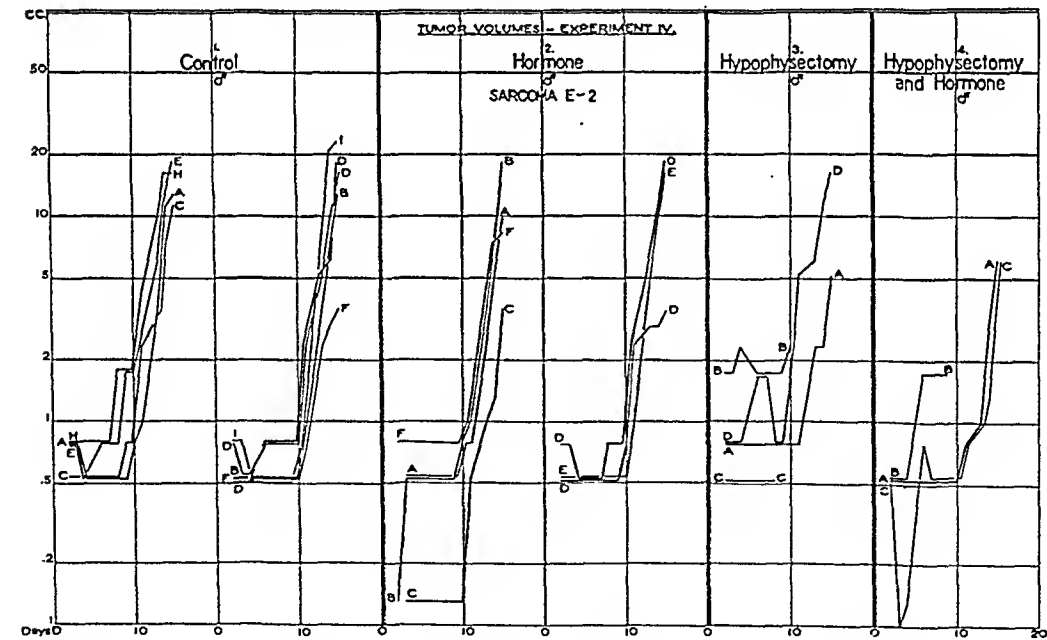


Chart 8.—Experiment 4. Tumor volume chart. Donor 32614 ♂, Sarcoma E-2. c.c. Tumor volume (according to prolate-spheroid formula). Days: Time from tumor implantation to removal. (See body weight chart of Experiment 4.)

animals "A" and "C" of Group 3 and "B" of Group 4 is not attributable to the growth of the tumors, since these particular tumors were exceedingly small at the time of removal.

On Chart 8 the tumor volume for each group is recorded in graphic form. The control and hormone groups produced tumors of approximately the same volume.

The completely hypophysectomized animals of Group 3 grew either insignificant or very small tumors. The partially hypophysectomized animal "D" conformed more closely to the controls. In Group 4, the completely hypophysectomized animals receiving growth hormone also grew insignificant or very small tumors, and the two partially hypophysectomized animals grew tumors less voluminous than the average control group. We may say, therefore, that in this experiment growth hormone did not increase the growth of the tumor, but that hypophysectomy inhibited the growth beyond that expressed by the progressive loss in body weight.

DISCUSSION

Notwithstanding the limited number of observations, our results were sufficiently uniform to permit certain deductions.

All of our tumor material was studied microscopically. In no instance did hypophysectomy or substitution therapy alter the cellular appearance or constituency.

With few exceptions, the comparative body weight changes of each group were practically the same. Growth hormone accelerated the weight increase of the control animals only very slightly or not at all. Complete hypophysectomy invariably arrested and decreased body weight. Only a few of the hypophysectomized animals increased in weight when given growth hormone, but the increase, with one exception, did not parallel that of the controls.

Variations in tumor volume occurred in each group studied. The very marked retardation of tumor growth in the hypophysectomized group in the last experiment is more striking than in the other three, and probably is due to the longer interval between hypophysectomy and implantation. It is interesting that distinct differences in growth behavior occurred in the two derivatives of Sarcoma E-5. These differences were not as markedly present in the Sarcoma E-2 derivatives. However, allowing for some unusual variations in Tumor E-5 in Experiment 2, the general growth potentialities were the same in all groups of all experiments. Only in Experiment 1, where a crude growth hormone extract of undetermined potency was used, a slight increase in volume gain over the control group occurred. It is more than likely that this hormone extract contained other pituitary factors, as pointed out in Experiment 1. This may explain the difference in tumor behavior in this group, because in all other experiments growth hormone substitution was not sufficient to overcome the deficiency set up by pituitary ablation, regardless of the dosage given. It was interesting, also, to note that hypophysectomy can affect tumor strains differently although they may be as intimately related as E-2 and E-5, which were derived from the same stem. Thus, in Experiment 2 the retardation of growth was far more apparent than in Experiment 3. In fact, in Experiment 3 the tumor volume of the hypophysectomized group nearly paralleled that of the controls, both treated and untreated. The same was true of Sarcoma E-5 in Experiment 1. On the other hand, in Experiments 2 and 4, Sarcomas E-5 and E-2 both

showed definite retardation of tumor growth. This suggested to us that even in tumors of the same cellular constitution and of common origin, the behavior of the individual derivatives may materially differ under identical conditions because of unknown changes in extrachromosomal influences.

We were surprised by the unusual behavior of the tumor implanted into hypophysectomized rats treated with growth hormone. We found that even fairly large doses failed to bring the tumor growth to normal, and in some instances it even dropped below that of the untreated animals. It may be reasonable to presume that the larger dosage of hormone exerted a toxic effect upon the tumor, although we could not prove this to our satisfaction by the microscopic studies. We are therefore at a loss for an explanation of this occurrence.

We may safely say that as far as the behavior of our tumors was concerned, the tumor volume paralleled that of the body weight increase except in a number of hypophysectomized animals. Here the tumor volume behaved erratically, showing definite retardation in some instances, and none in others. It is also interesting that tumors showing retardation did so to a lesser degree than was expected from the behavior of body weight.

That tumor growth was retarded but not arrested in hypophysectomized animals, and that tumor growth progressed out of proportion to the loss of body weight of the host are shown in Table I. This was true of both strains of sarcoma, although there were again evident differences between E-2 and E-5. We realize that the figures for hypophysectomized animals implanted with Sarcoma E-2 allow a wide margin for error, for it is quite probable that with a larger series the figure for daily tumor weight gain would have been greater but probably still below that of normal animals, as in E-5, shown on the same chart. Nevertheless, the fact remains that the hypophysectomized animals not only lost weight ordinarily, but they also grew less tumor than the controls, although marked variations of growth behavior occurred.

We believe that our transplantable sarcoma is dependent only to a limited degree upon the hypophysis. We believe, also, that its growth is not increased by the administration of growth hormone, and that, even after discontinuance of pituitary secretion, the tumor may follow inherent growth propensities but may be impeded by an altered metabolism.

We are in agreement with McEuen and his coworkers, and others, that hypophysectomy retards, and at times arrests, tumor growth, depending to some extent upon the time relation between hypophysectomy and tumor implantation. Judging solely from our own experience, we have no reason to believe that malignant cells are necessarily more sensitive to pituitary influences, as suggested by Ball and Samuels,

although in their experiments an autogenous fibrosarcoma and a Walker carcinosarcoma showed striking retardation in hypophysectomized animals. It will be necessary to study the behavior of many different tumors and tumor strains before this statement can be accepted as applicable to all malignant cells. On the other hand, our experiments bear out their belief that under normal conditions available pituitary secretion is at a maximum and that the addition of growth hormone will not increase the inherent growth rate of tumors.

TABLE I. DAILY TUMOR AND BODY WEIGHT CHANGES OF 60-DAY MALE RATS*

CONTROL SERIES			HYPOPHYSECTOMIZED SERIES		
ANIMAL NO.	DAILY TUMOR WEIGHT GAIN GM.	DAILY BODY WEIGHT CHANGE GM.	ANIMAL NO.	DAILY TUMOR WEIGHT GAIN GM.	DAILY BODY WEIGHT CHANGE GM.
<i>Implanted With Sarcoma E-2</i>					
1220	0.634	+2.34	1213	0.708	+1.30
1221	0.591	+2.17	1218	0.304	-0.30
33178	0.586	+3.07	33182	0.157	-1.07
33184	0.451	+2.28	33193	0.074	-1.33
33196	0.473	+2.10	33206	0.050	-2.85
33217	0.642	+2.64			
33220	0.732	+4.00			
33233	0.175	+1.00			
33245	0.677	+4.07			
33271	0.650	+3.78			
33275	0.895	+3.35			
Group Av.	0.591	+2.80	Group Av.	0.258	-0.85
<i>Implanted With Sarcoma E-5</i>					
32101	0.012	+2.31	32102	1.066	-0.02
32116	2.000	+2.81	32104	0.714	-1.81
32136	0.058	+2.62	32114	0.256	-0.06
32432	1.411	+2.50	32137	1.019	-0.25
32434	0.658	+2.12	32141	0.025	-0.62
32452	1.578	+1.62	32099	0.228	-0.37
32467	0.507	+1.43	32448	0.312	-1.62
32455	1.062	+2.62	32454	1.000	-0.62
32496	0.480	+3.06	32458	1.462	+0.31
			32466	1.062	0.00
Group Av.	0.862	+2.35	Group Av.	0.714	-0.51

*Animals of Experiments 1 and 4 implanted with Sarcoma E-2. Animals of Experiments 2 and 3 implanted with Sarcoma E-5.

The interesting work of Bischoff and his coworkers, showing that severe irradiation of the hypophysis will retard tumor growth to the same extent as hypophysectomy, has not yet been repeated by us. Their observation that growth retardation can be offset to some degree by growth hormone substitution was observed by us only in a few instances.

We agree with McEuen and others, and Franseen and McTiernan, that there exists a relation between the pituitary gland and tumor growth, but we believe that it does not materially differ from the somatic response of the tumor host.

CONCLUSIONS

1. Allowing for known variations, the administration of growth hormone did not increase the growth propensities of our autogenous rat Sarcomas E-2 and E-5.

2. Growth hormone administered to hypophysectomized rats failed, in most instances, to stimulate tumor growth to the normal rate.

3. Complete hypophysectomy affected the growth of our tumors variably. In most cases, growth continued normally. Retardation was slight, and complete arrest only rare. The greatest retardation occurred when the interval between hypophysectomy and tumor implantation was lengthened.

4. Hypophysectomy or the administration of growth hormone failed to change the cytologic appearance of the tumors studied.

We gratefully acknowledge the services of Dr. P. E. Hoffmann, who performed all of the hypophysectomies for this study.

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DISCUSSION

DR. SAMUEL H. GEIST, NEW YORK, N. Y.—It is apparent from the presentation of Dr. Emge's paper that the question of the relation of hormones to tumor growth is a complex one. Two aspects of the problem immediately present themselves. One is the effect that must be exerted on normal quiescent cells to change them into abnormal ones. The second is the effect on such cells to increase their growth rate. These are two entirely separate problems.

Hofbauer had the idea that the pituitary hormone was involved in the first of the two actions, and to support his contention transplanted the eosinophilic portion of the

pituitary to animals and observed changes in the cervix that he thought were suggestive of neoplasm. We are not at all convinced that they represent neoplastic changes.

It is known that certain substances called carcinogenic can stimulate tissues to such an extent that typical tumor growth will result. Such experiments were done on rabbits using a tar preparation as the carcinogenic agent. The tar preparations, clinically, seemed to be very closely related to estrogenic substances. Engel was successful in producing lesions in the cervix that resembled early carcinoma by injecting monkeys with estrogenic substances, but in his cases the cervix had previously been traumatized. Apparently there was more than one factor responsible.

Second, as to the growth-stimulating factor, it does not seem that the hormone itself can be entirely responsible. In gigantism while there is an excessive rate of growth there is nothing suggesting malignancy. The same thing is true if one gives to an immature animal growth hormone. The animal grows rapidly but does not develop a malignant tumor. If the hormone is concerned with malignancy, there is some other factor that sensitizes the cells to respond. Some men have found that by hypophysectomizing animals the growth is retarded and if the hormone is given, contrary to the results that Dr. Emge obtained, the growth is again stimulated to develop.

I have had occasion to examine 250 pituitaries from a large group of patients who had died from various causes. My interest was centered more in the morphologic changes that occurred in the various ages and sexes. Among the 250 there were 37 glands obtained from patients who had died of carcinoma of various types. Histologic study failed to show any changes in the eosinophilic portion that could not be accounted for by the variation in age or sex. Of course, one could immediately say that it is perfectly possible for a cell to have a functional disturbance without recording it in a morphologic change.

Hofbauer made the suggestion that, because of the effect that the growth hormone had on tumors, by decreasing the pituitary activity one might get better results than by simple operation alone. Recently several papers have appeared from German clinics in which the authors stated that the results obtained in carcinoma of the uterus are somewhat better if a combination of pituitary x-ray and surgery is employed than by surgery alone. That, of course, remains for the future to prove.

Sarcoma is apparently not so susceptible to the effects of the growth hormone, and likewise transplanted tumors do not show the same response as do spontaneous tumors.

Dr. Emge's results seem to indicate that there is no relation between growth hormone and malignant changes. Of course, the problem being so difficult, it is unfair to conclude that there is no relation. Such experiments as Dr. Emge's should be persisted in.

DR. EMIL NOVAK, BALTIMORE, Md.—There is at present much interest in the question of the possible relation of hormones to tumor growth, and especially of the estrogenic substances to cancer. There has always been a rather deep-seated, almost traditional feeling that tumors are in some way brought about by a disturbance of growth phenomena. The older concept was that a tumor consists of cells in which growth propensities have got the upper hand, while other cell functions have retrogressed. As regards cancer, the further generalization was drawn that the growth balance between the different types of tissue was disturbed, so that, for example, an abnormally growing epithelium could melt down the normal barriers between epithelium and connective tissue and thus assume invasive characteristics. Vague and speculative as these hypotheses were, they lend added interest to Dr. Emge's work, in which an attempt is made to throw light on the influence of the growth hormone

upon tumor growth. His results, as you have heard, have been in the main quite negative.

As regards Dr. Emge's method of attacking the problem, two comments suggest themselves to me. The hormone preparations with which he worked contain not only the growth hormone, but also at least small amounts of the sex hormone, and at least traces of protein. Since in spite of this, the preparations produce definite growth changes in laboratory animals, and since Emge's results on tumor growth were so unimpressive, this objection does not vitiate his results.

More important, perhaps, is the fact that he used hypophysectomized animals for his study. When hypophysectomy is done, one removes not only the growth principle but many others of profound importance to the body, such as the thyrotropic and adrenotropic principles, the sex hormones, and several others, and this must produce a profound effect upon the nutritional functions, an effect perhaps comparable to that seen in cachexia hypophyseopriva or Simmond's disease, in which the constitutional depravity is so extreme that death almost always ensues. Quite a number of Dr. Emge's hypophysectomized animals died, as he has said, and in those which did not it would seem that the nutritional upset would blur and confuse the interpretation of results. Only the growth hormone, presumably, was put back into the animals' circulation whereas a number of vital principles had been removed by the hypophysectomy.

For this reason, it would seem to me that other methods of study of this problem, such as the investigation of the effects of various hormones upon tissue cultures of tumor cells, might be more productive of definable results.

DR. EMGE (closing).—No doubt there remains much more to be said which must wait until our investigation has progressed sufficiently to permit broader deductions. At this moment our results must be interpreted within the strictest confine of this highly specialized field of investigation.

I fully realize that this sort of research is looked upon by many as of no particular value because results are not at once applicable to clinical medicine. Yet more information gathered in this fashion may ultimately yield information highly acceptable to the clinician. Our ultimate hope is to shed some light upon the question whether or not there is a relation between tumor growth and the endocrine system. It will answer a very important question and that is, are we safe in administering large doses of hormonal substances over long periods of time without awakening dormant carcinomorphic elements?

Clauberg, C.: Unusual Gynecologic Findings in Children, *Deutsche med. Wchnschr.* 61: 1668, 1935.

Occasionally a malignant tumor or a foreign body furnish the cause for a persistent vaginal discharge in a child, as for instance, in the case of a four-year-old girl who rapidly succumbed to a malignant angioendothelioma of the vagina in spite of radium treatment.

Foreign bodies were detected in two other cases: A girl of six masturbated with a slate pencil, and in a girl of eight, small pebbles and two safety pins, one of which was opened, stayed in the vagina for over a year. The hymenal opening was very small and prevented a thorough examination. A surprisingly good view could be obtained through a small cystoscope after ballooning the vagina with water.

A case of severe inpaling injury is also reported where the complete transverse separation of vagina and urethra could be detected only after an extensive Schuchardt-Duehrssen incision; while vulva and hymen showed nothing but contusions.

G. E. GRUENFELD.

ESTROGENIC SUBSTANCES IN THE BLOOD OF WOMEN

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A SIMPLE procedure for the demonstration of estrogenic substances* in blood was described in two previous communications (Fluhmann^{1, 2}). This test depends on the induction of "mueification" of the vaginal epithelium of adult spayed mice by the injection of untreated blood serum, and has now been employed in more than 1,000 instances in the Stanford Gynecological Laboratory. The present report is a further analysis of our experiences with this method and its application to the study of various menstrual disorders.

TECHNIC

A few changes have been made in the technic of the test since it was first employed, the most important of which is a shortening of the period of injection from seventy-two to forty-eight hours.

The blood is obtained by venipuncture and immediately placed in a test tube for transmission to the laboratory. From 25 to 40 c.c. are taken each time. The clear serum is secured by centrifugalization, and the cells are discarded. If it is kept sterile, the serum may be left in the ice box for days and even weeks without losing its potency.

The animals used are adult female mice† which have been spayed six to seven days prior to the day the test is begun. This is important, for if the period of castration is shorter the vaginal mucosa may show unusual changes difficult of interpretation at the end of the test, while if it is longer the mice are not as sensitive to the action of estrin. The usual procedure has been to do a bilateral oophorectomy on the mice on a Tuesday and to begin all tests on the same day of the following week.

A total of 4.5 c.c. of blood serum is given to each mouse, and the test is completed in forty-eight hours. The serum is administered subcutaneously in the back, and the site of each injection is varied as much as possible to facilitate absorption. Three injections of 0.75 c.c. are given daily, at 8:00 A.M., noon, and 5:00 P.M., for two consecutive days. On the third morning the animal is sacrificed and the vagina is carefully dissected free. This is a simple procedure and is accomplished by first making a long incision in the abdominal wall and separating the symphysis pubis. The vagina is fixed in formalin, mounted in paraffin, and transverse sections are made at different levels and stained with hematoxylin-eosin.

The changes elicited in the mouse vagina were previously described with complete photomicrographs (Fluhmann²). According to the amount of estrin present, six reactions are recognized:

Reaction 0: Atrophy of the vagina. Mucosa shows two layers of low cuboidal epithelium. Occasional leucocyte.

*The terms "estrin," "estrogenic hormone," and "estrogenic substances" are used synonymously in this report as generic names for the hormone or hormones in the blood of women which induce estrous changes in the vagina of the spayed rodent. The exact chemical nature of these factors has not as yet been determined.
†Since mucification in rats does not develop as readily as in the mouse, they are not suitable animals for this test.

Reaction 1: Vaginal mucosa shows two layers, a basal of low cuboidal epithelium and a superficial of tall columnar cells. A few leucocytes.

Reaction 2: The superficial cells are high, begin to show stratification, and secrete mucus. There is a well-marked increase in leucocytes which may also be found in the lumen of the vagina.

Reaction 3: The epithelium of the vaginal mucosa is composed of several layers, and the cells at the surface are of the mucified variety. A characteristic feature often observed is a folding-in of the mucosa, a type of festooning, which is evidence of rapid growth. The mucosa is invaded by large numbers of leucocytes which also occur in the lumen along with epithelial débris.

Reaction 4: The mucosa is made up of from 6 to 8 or 10 rows of cells, the lower resembling the basal cells of squamous epithelium while those at the surface are still of the tall mucified variety. Leucocytes have disappeared, or are present in small numbers.

Reaction 5: The vagina is now lined by fully developed squamous epithelium with cornified cells at the surface. There are no leucocytes. Since the test is completed in forty-eight hours, a reaction given as 5 may consist of mucified cells at the surface, with cornification just appearing between the surface and the lower stratified layers.

As in all biologic procedures, individual mice vary greatly in their responses to the same dosage, and in this work two or three mice were the minimum employed for each test. After the response for each mouse has been estimated, the numbers are added and then divided by the number of mice used in order to give the reaction. For instance, if three mice are used for a test and reactions 3, 3, and 2 are observed, the reaction elicited by that specimen would be given as 2.7, or three-plus.

On the basis of tests performed with known amounts of estrogenic substance (theelin—Parke, Davis & Co.), and since Kemp and Bjer-gaard³ showed that estrin is equally distributed between the red blood cells and the plasma, the average reactions in terms of mouse units per 100 c.e. of whole blood are roughly interpreted as follows:

Average reaction	0 to 1.0	= negative
Average reaction	1.1 to 1.5	= one-plus = traces of estrin
Average reaction	1.6 to 2.4	= two-plus = ± 3 M.U. per 100 c.e.
Average reaction	2.5 to 3.4	= three-plus = ± 6 M.U. per 100 c.e.
Average reaction	3.5 to 4.4	= four-plus = ± 12 M.U. per 100 c.e.
Average reaction	4.5 to 5.0	= five-plus = ± 24 M.U. per 100 c.e.

ACCURACY OF TEST

The chief sources of error in the use of the test arise from the variations that occur in the responses of individual mice, and the problem of correctly interpreting the degree of change induced in the vaginal epithelium. The first difficulty is offset by employing as many animals as the amount of blood serum will allow, and the second by having all the tests judged by a single observer. It is desirable that a proper standard be established, and anyone desiring to conduct this test should first study a large series of mice injected with known amounts of estrin at various dose levels.

In order to determine the sensitivity of the test, a series of 94 mice was injected with known amounts of theelin (Fluhmann²). The result proved very satisfactory, and as a further check, a second series of 63 animals was recently similarly treated. The theelin was given in aqueous solution at different dose levels, and the injections were conducted in the same manner as in the tests with human blood. The results are given in Table I. It is seen that a dosage of one or two mouse units uniformly

TABLE I

DILUTION	MOUSE UNITS	REACTIONS										AV. REACT.	
C	2	5	5	5	5	5	5	5	5	5	5	5.0	
D	1	5	5	5	5	5	5	5	5	5	5	5.0	++++
E	1/2	4	4	4	4	3	4	3	4	2	2	3.6	+++
F	1/4	2	4	3	3	4	3	4	2	3	2	3.0	+++
G	1/8	2	3	2	2	3	2	1	2	1	1	1.9	++
H	1/16	2	0	1	1	1	1	1	2	2		1.2	+
	0	1	1	1	0	0						0.6	0

gave reaction 5; one-half mouse unit gave an average reaction of 3.6 (four-plus); one-fourth unit elicited an average reaction of 3.0 (three-plus); one-eighth unit, average reaction of 1.9 (two-plus); one-sixteenth unit, average reaction of 1.2 (one-plus); and five uninjected controls gave 0.6 (negative). A study of the responses in individual mice shows that a high degree of accuracy may be obtained even when only two or three animals are employed, and also that the number of errors increases as the dosage of estrin diminishes.

RESULTS

The present study is based on 401 determinations which have been conducted in 84 women and 15 prepubertal girls, and does not include cases previously reported. The patients, unless otherwise stated, had no organic pelvic disease but were under the care of the Endocrine Division of the Women's Clinic for various "functional disorders." With the exception of the group of preadolescent children, a series of examinations was made in each case at intervals of from three to ten days in order to establish a "blood-estrin curve." The arrangement of the cases in this report was made according to the menstrual history rather than the clinical diagnosis, since this gave a greater uniformity in the results.

PREPUBERTAL GIRLS

The blood of 15 normal girls varying from four to ten years of age was examined for the presence of estrin by the mucification test. The results are given in Fig. 1, and it is seen that they are very consistent. Of 8 children seven years of age or younger, only one, a girl of seven, gave a positive reaction. On the other hand, 7 blood tests in girls eight to ten years of age gave a two-plus reaction in 5 instances, a one-plus once, and a negative once. These findings are significant because secondary sexual characteristics appear between the ages of eight and ten years. At this time the differentiation of the female pelvis begins and there is also the growth activity of the mammary tree, which precedes the gross development of the breasts (Howard⁴).

MENSTRUAL CYCLES OF TWENTY-FIVE TO THIRTY DAYS IN LENGTH

This group is composed of a series of 12 women whose menstrual cycles, at the time of examination, were twenty-five to thirty days in length. A total of 14 blood estrin curves based on 62 tests are available for study. Seven of the patients complained of dysmenorrhea, one of dysmenorrhea and sterility, one of irregular delayed menses, one of polymenorrhea, one of underdevelopment of the breasts, and one was a normal control.

In a previous report (Fluhmann²) a composite curve, based on the examination of 80 specimens obtained from 46 patients at various stages of the cycle, showed an increase in the amount of estrin in the blood during the midinterval, with a secondary rise at the time of menstruation. This result has been accepted as the normal, and a study of the individual blood estrin curves in this group shows a close agreement with this standard. In spite of wide variations, the most constant finding was that of a rise in the concentration of estrin in the blood occurring from

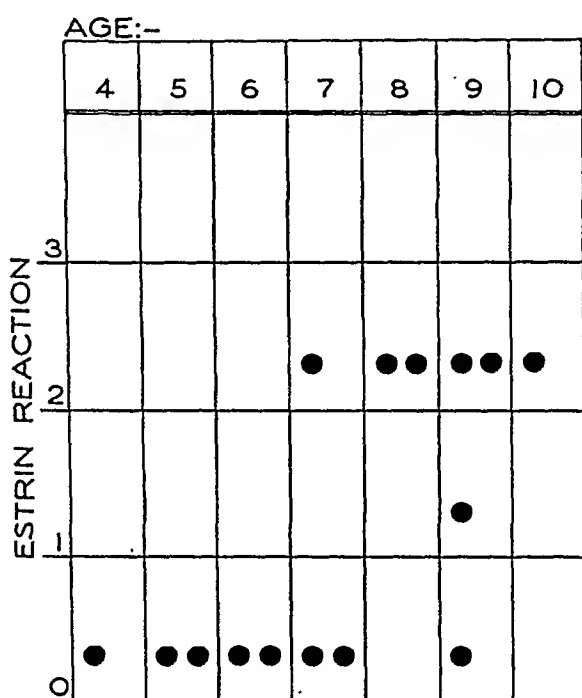


Fig. 1.—Estrogenic substances in the blood of 15 prepubertal girls.

eight to eighteen days before the onset of menstruation (Figs. 2 and 3). This peak was noted in 11 out of 14 curves, and in addition a secondary increase within four days or actually at the time of menstruation was observed in 5 of these cases (Fig. 3). In 2 instances, the only rise was found during the three days preceding menstruation, and in one traces of estrin or negative tests were obtained throughout the whole cycle.

One patient became pregnant while a series of tests was being conducted. A negative result was obtained on the sixth day, a two-plus on the twelfth and eighteenth days, negative on the twenty-sixth day, and finally a four-plus on the sixty-fifth day following the first day of the previous menses.

It would seem that these results are not in keeping with the blood estrin studies of Frank and Goldberger,⁵ Mazer and Goldstein,⁶ Siebke,⁷ and others. These authors, who employ a method based on the chemical extraction of estrin from the blood, find a consistent positive test only during the seven days preceding the menses, while it is not demonstrable at other times. The rise in the midinterval

and the secondary increase just before or at menstruation, which have been observed with the mucification test, however, show much similarity with the total daily urinary excretion of estrin at various stages of the cycle. For instance, Loewe and Langes noted an increase in the urinary excretion ten to twelve days after menstruation. Frank⁹ states, "considerable variations are encountered, but two periods of maximum excretion, the first corresponding to the theoretical time of full follicle ripening

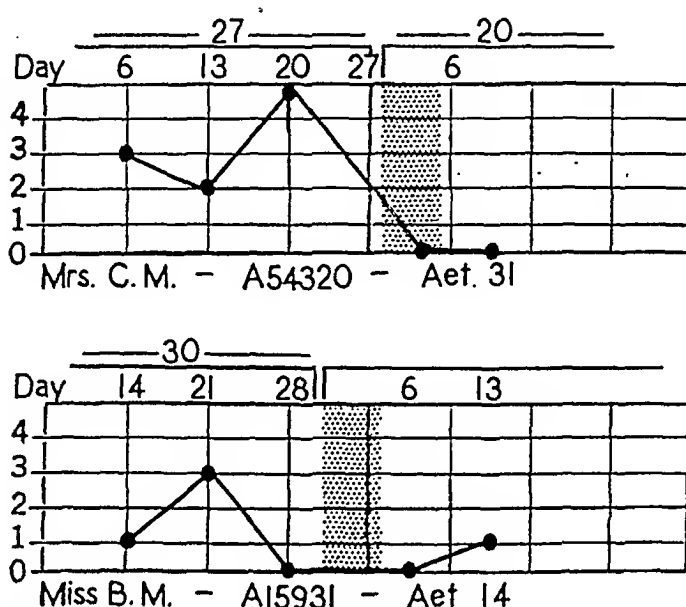


Fig. 2.—Blood estrin curves of patients with menstrual cycles twenty-five to thirty days in length.

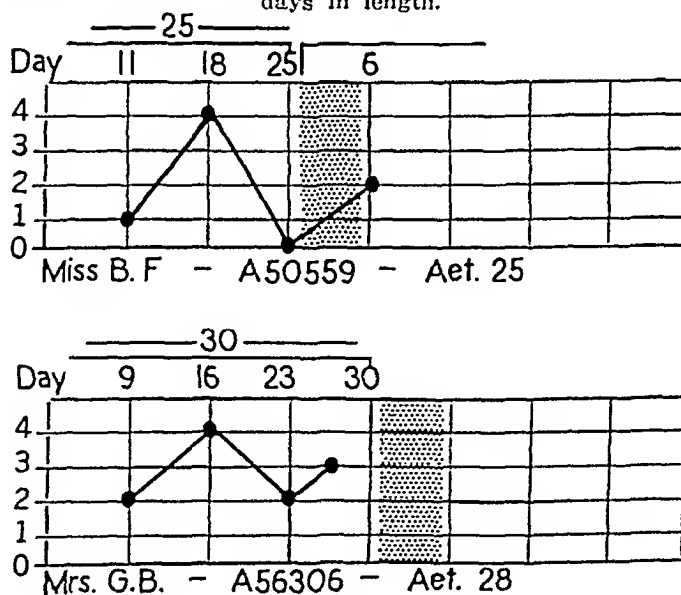


Fig. 3.—Blood estrin curves of patients with menstrual cycles twenty-five to thirty days in length.

or ovulation (fourteenth day), and the second in the last week preceding the menses, are characteristic." Siebke⁷ found the highest excretion ten and eleven days before menstruation. The figures given by Zondek¹⁰ for the various stages of the cycle show the highest amounts (300 mouse units per liter) from the nineteenth to the twenty-first days as compared with 50 to 70 units at other times. In a recent study, conducted with one subject over a period of some months, Gustafson and

Green¹¹ found an increased estrin content in the urine from the ninth to the twelfth days following menstruation, and a secondary rise from the fourteenth to the twenty-first days.

MENSTRUAL CYCLES OF THIRTY-ONE TO FORTY DAYS IN LENGTH

Thirty-eight tests were performed on 8 patients with menstrual cycles ranging from thirty-one to forty days in length. Three of these patients reported for investigation with the complaint of "irregular delayed menses," three complained of sterility, and two of dysmenorrhea.

A midinterval increase in estrin concentration was observed in every case (Fig. 4). In 2 instances it was found on the seventh and eleventh days, respectively, before menstruation, while in 6 it varied from fourteen to twenty-one days before the succeeding period. A secondary rise occurred on the first day of the menses in one case. The curves in this group thus conform to those of women with cycles of twenty-five to thirty days in length, but the greatest concentration was found somewhat earlier in the interval.

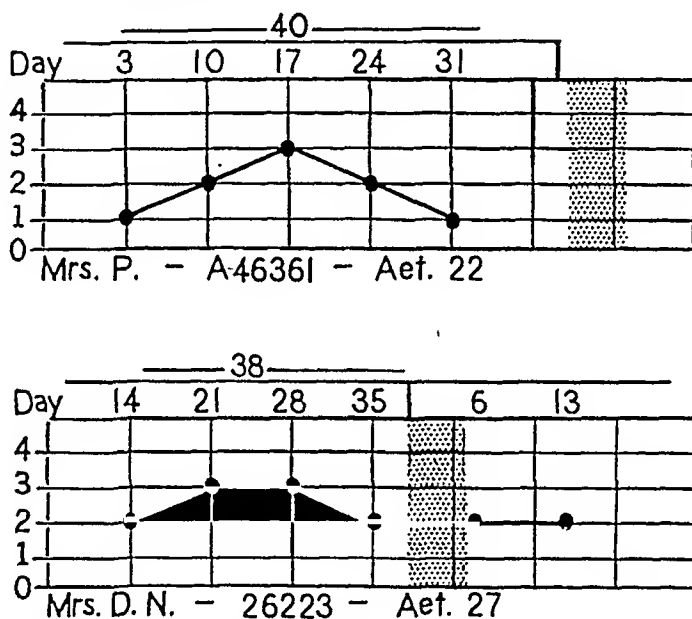


Fig. 4.—Blood estrin curves of patients with menstrual cycles thirty-one to forty days in length.

SCANTY MENSTRUATION

Four patients with cycles varying from twenty to thirty-six days in length complained of "scanty menses." Fifteen tests were performed and again a constant midinterval rise in estrin concentration was observed, while one patient showed a premenstrual rise which occurred on the last day of a twenty-two-day cycle. No indication was found that such cases should be considered as "hypoovarian" in the sense that smaller quantities of estrogenic substances are found in the blood.

ANOVULATORY CYCLES

It was hoped that a large series of patients with "anovulatory cycles" could be studied from the standpoint of estrin content of the blood, but technical difficulties made it a very elusive task. The diagnosis is dependent on demonstrating an "estrin phase" in the endometrium just before or during an apparently normal menstrual period, and since the tests must be performed in the weeks preceding the

actual flow, the choice of patients became a question of guesswork or chance. It also seemed correct to eliminate from this group individuals with profuse bleeding who showed a characteristic hyperplasia endometrii. For these reasons, only four patients were available, and in each case the diagnosis of "anovulatory cycle" was made from the examination of biopsy specimens of the endometrium obtained just before or at the onset of a period of bleeding which to patient and doctor seemed to be a "normal menstruation" at the expected time. The specimens of endometrium were obtained with a Hoffmann curette¹² and we believe that the bleeding was not an unusual event precipitated by this minor operative procedure.

Fourteen tests were done on the four patients, but the curves do not show any consistent pattern which can be considered characteristic for this type of cycle. In

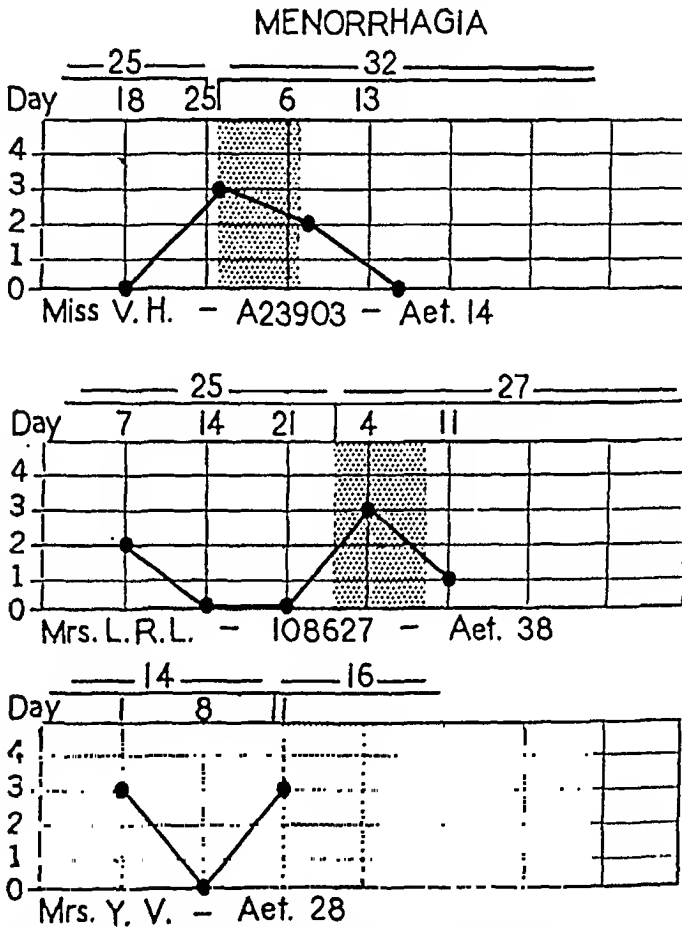


Fig. 5.—A characteristic of the blood estrin curves of some patients with menorrhagia or polymenorrhea is an increase in the concentration of the hormone at the time of onset of the bleeding.

one case three tests were negative or showed merely traces of estrin. A second gave two-plus and three-plus reactions on the fourth, thirteenth, and twenty-fifth days of a twenty-seven-day cycle. The third gave a rise in estrin concentration three days, and the fourth fourteen days, before the onset of menstruation. The findings must therefore be considered as inconclusive.

MENORRHAGIA AND POLYMENORRHEA

Seven patients complaining of profuse menstrual periods were examined, and of these, 3 were young girls of thirteen to seventeen years of age. Thirty tests were performed, and of the 7 blood estrin curves, 5 showed a striking picture which

differed from the normal standard. The peak of estrin concentration was found associated with the onset of the bleeding and then gradually decreased as the flow diminished (Fig. 5). Of the two exceptions presenting the normal midinterval rise in estrin concentration, one was a patient in whom the bleeding was attributed to an old pelvic inflammatory disease and not to a "functional disorder."

Four patients complained of polymenorrhea, cycles shorter than twenty-five days, in addition to profuse flow, and 15 tests were conducted in this group. Two of these again showed a marked increase in the amount of estrin in the blood at the time of the onset of the bleeding (Fig. 5).

HYPERPLASIA ENDOMETRII

Twenty tests were conducted in 5 patients with irregular or profuse uterine hemorrhage associated with the histologic picture of hyperplasia endometrii. In 3 cases the blood estrin curves showed a sharp rise in concentration at the time of onset of the bleeding and a decrease with the cessation of the flow. One patient was examined

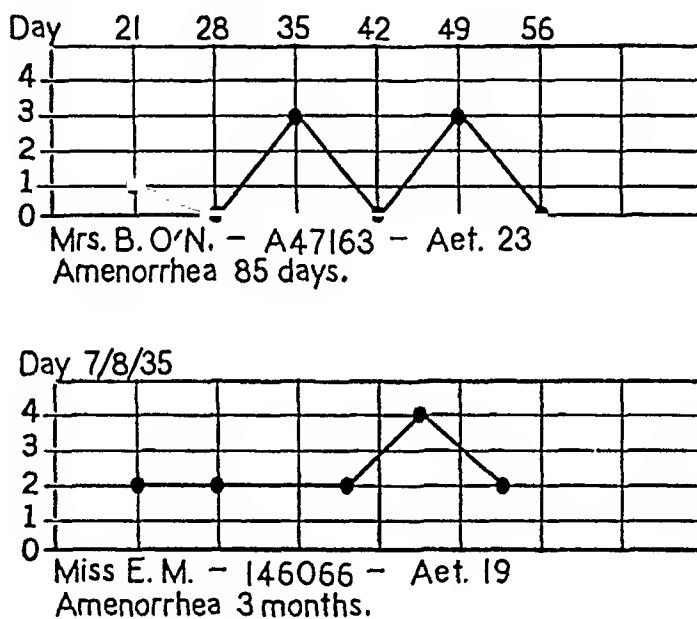


Fig. 6.—Type I curves of patients with amenorrhea.

sixteen days and eight days before the onset of a profuse period and showed a one-plus and a negative reaction. In another case, 3 tests demonstrated a sharp increase in the estrin content over a period of five days following a curettage, but no subsequent history is available.

The results of the blood examinations in this group and in the patients with menorrhagia suggest that certain cases of "functional" uterine hemorrhage are associated with an increase in the concentration of estrogenic hormone in the blood at the time of the onset of the bleeding. These findings are confirmatory of the blood studies of Siebke and the urine determinations of Frank and others.¹³

AMENORRHEA

This group represents the largest of this series and consists of 119 tests, 26 blood estrin curves from 22 patients. The association of other hormonal tests and clinical findings with the estrin studies is reserved for a future publication, but the results fall into three distinct groups:

1. *Type I Curves (Cyclic).*—In this category are 16 curves from 13 patients in whom there was a recurrent increase and decrease in the amount of estrogenic substances in the blood (Fig. 6). The rise generally occurred every two to three weeks and was as great as that observed during the midinterval in normal individuals. In 8 cases a period of uterine bleeding set in either during the period of observation or

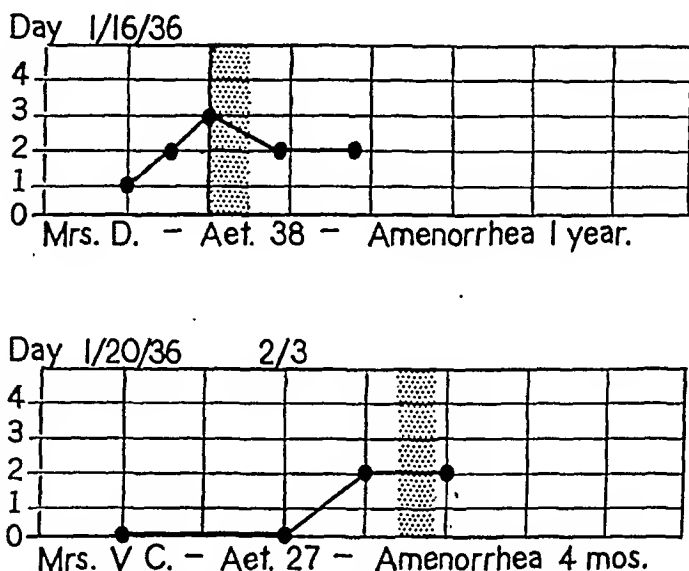


Fig. 7.—Curves illustrating increase in the concentration of estrin in the blood at the onset of uterine bleeding following a period of amenorrhea.

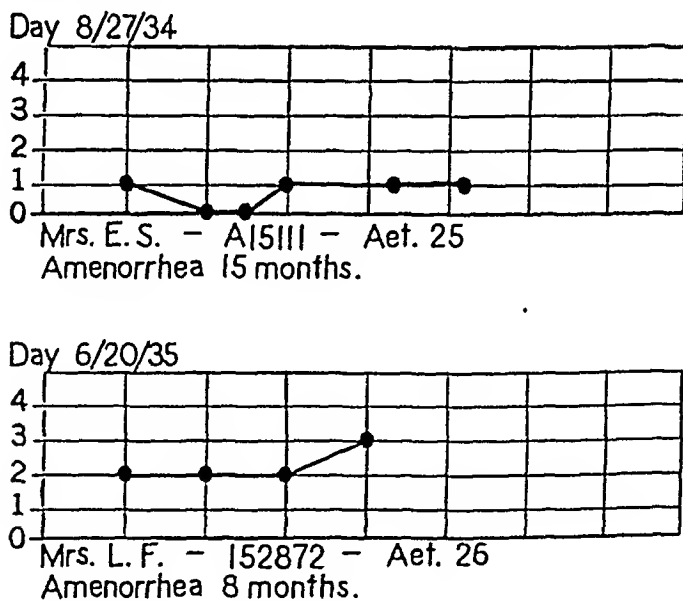


Fig. 8.—Type II and Type III curves in amenorrheic patients.

shortly afterward, and in 4 patients there was a rise in estrin concentration associated with the onset of the flow (Fig. 7). This observation may mean that such bleeding following amenorrhea does not necessarily represent a normal menstrual period, but an abnormal uterine hemorrhage.

2. *Type II Curve.*—In 4 instances no clear cycle could be demonstrated, but all tests gave a two-plus reaction with an occasional increase to three-plus or a decrease to one-plus or negative (Fig. 8). These patients therefore must be considered

as having a small but appreciable amount of estrogenic hormone constantly present in the blood. Of special interest in this group was a patient with an amenorrhea of seven and one-half years' duration, attributable to a hypophysial tumor associated with acromegalic changes.

3. *Type III Curve.*—This group is illustrated by 6 blood estrin curves (5 patients) in which reactions 0 and one-plus were found in all tests, with only an occasional exception (Fig. 8). The amenorrhea is thus associated with a persistent absence of estrin from the circulating blood. The only case of primary amenorrhea in this series, a patient of Dr. R. Glenn Craig, belongs to this category, and is illustrated in Fig. 9. It is interesting that the administration of a pituitary gonadotropic hormone (Prephysin-Chappel) resulted in a sharp rise in the blood concentration which persisted for two weeks. However, menstruation did not ensue and 3 successive tests gave negative findings.

The patients with amenorrhea of longer and shorter duration may thus be divided into 3 groups according to the blood estrin determinations. In the majority

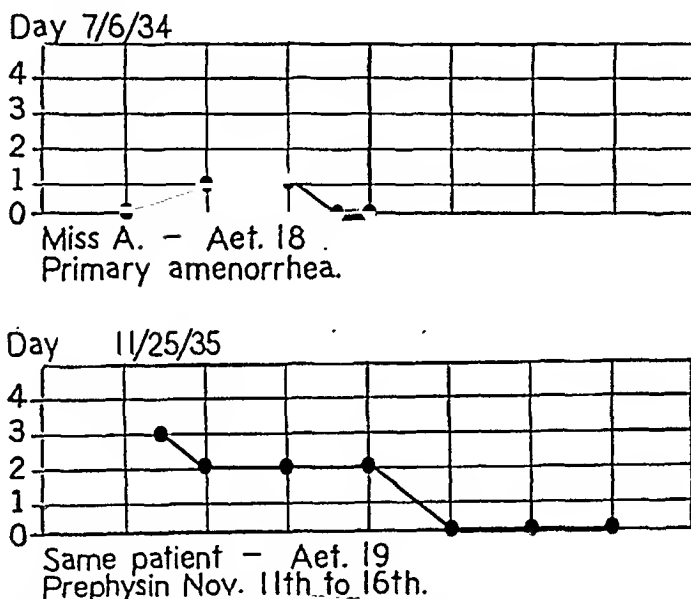


Fig. 9.—Patient with primary amenorrhea. Type III curve with increase in blood estrin following administration of a pituitary gonadotropic preparation.

there is a cyclic rise and fall in the amount of estrin present; in a smaller group there is a constant moderate amount of estrin in the blood; and in a third category are women with a total absence of demonstrable estrogenic hormone.

POSTCASTRATION

Since it has been assumed that estrogenic substances are primarily "ovarian hormones," it was of special interest to study the blood of women in whom bilateral oophorectomy had been performed. Twenty-eight tests were conducted on 8 patients, 5 of whom were under the age of forty and 3 from fifty to fifty-two years old. The time from the operation to the period of observation varied from five weeks to ten years. In all cases it was possible to demonstrate the presence of estrin in the blood in amounts comparable with those seen in normal individuals (Fig. 10). A cyclic increase and decrease of the hormone was noted in 4 cases, while in 4 the blood showed two-plus and three-plus readings, such as noted in the Type II curves of the amenorrheic patients. Although these results may seem startling, they are again in conformity with reports on the presence of estrin in the urine of castrates (Loewe and others,¹⁴ Laroche and others,¹⁵ Frank and others,¹⁶).

MENOPAUSE AND POSTMENOPAUSE

Sixteen observations were made on 3 patients complaining of menopausal vasomotor symptoms, in whom the menstrual periods were scanty or occurred at delayed intervals. In all instances a cyclic rise and fall of estrin was demonstrable, and

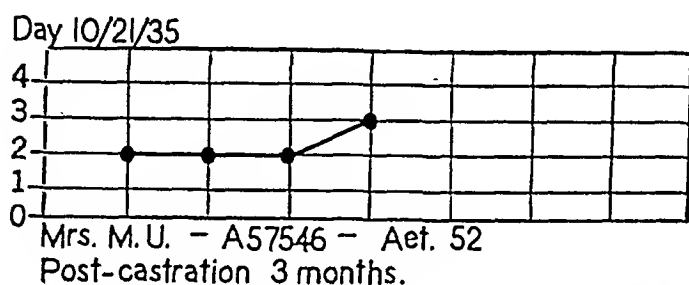
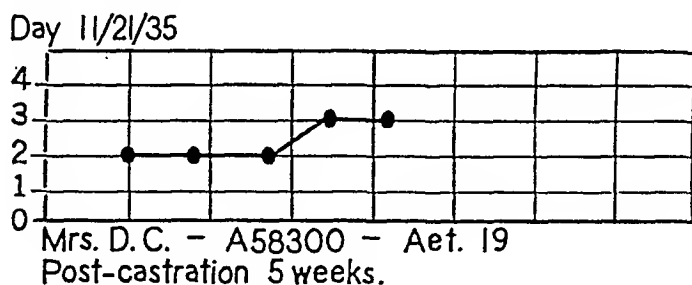


Fig. 10.—Estrogenic hormone in the blood of women following bilateral oophorectomy.

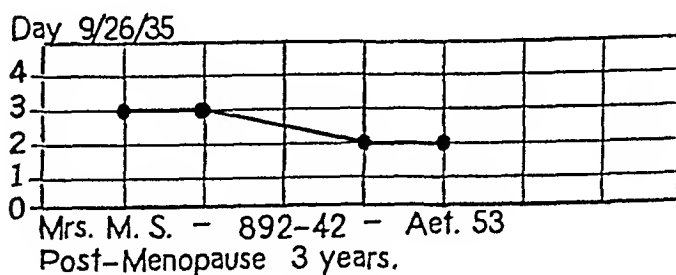
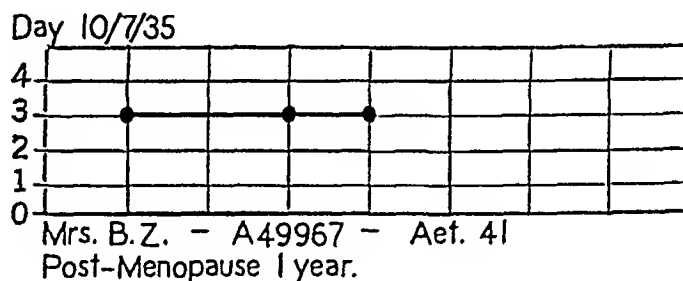


Fig. 11.—Estrin in the blood of women in the postclimacteric period.

although some irregularities were noted in the curves the observations are too few to determine any definite abnormality. It is interesting that 2 out of the 3 patients showed an increase in the amount of anterior pituitary hormone in the blood when tested with immature mice by the method previously described (Fluhmann¹⁷).

Nine tests were done on 2 patients with menopausal symptoms in whom a unilateral oophorectomy had been previously performed. In both instances a cyclic

occurrence of estrin, with peaks of three-plus, was demonstrated and in one there was also an increase of anterior pituitary hormone.

Fifteen tests were conducted on 4 patients who had passed the menopause from one to three years. In corroboration of the studies made with urine by Zondek,¹⁰ Kurzrok and Ratner,¹⁸ and Frank and others,¹⁶ it was possible to demonstrate appreciable amounts of estrin in the blood. In two cases the curves showed the presence of a cycle, while in two the results gave two-plus and three-plus reactions as in the Type II curve of the amenorrhoeic patients (Fig. 11). A positive test for the anterior pituitary gonadotropic factor was obtained in two patients whose blood was examined for this hormone.

DISCUSSION

One of the important developments of modern endocrinological investigation has been the use of various tests for the presence or absence, increase or decrease, of hormones in the blood, urine, or tissues. In the case of the Aschheim-Zondek test for the chorionic gonadotropic hormone, the results have been of invaluable assistance in the management of certain clinical problems. The methods which have been described for determining the presence of anterior pituitary sex factors and estrogenic substances have not proved of such practical value, but they have furnished new ways of studying the physiology and pathology of the reproductive cycle.

The Allen-Doisy test for estrin is a well-established laboratory procedure, but the relatively small amounts of hormone in blood or urine require chemical extraction before the biological examination can be conducted. In the case of blood, this means a laborious preparation which yields sufficient material to inject only one or two test animals. These difficulties call for a more efficient and less complicated procedure, and although the "mucification test" also presents disadvantages it may be considered as an alternative method.

It is difficult at present to reconcile the differences which this test has given when compared with the results obtained with the Frank-Goldberger method. It is possible that some explanation will be found when further chemical analyses are available, but, as pointed out previously, there are a number of important observations which suggest that the blood estrin curves obtained with the mucification test compare more favorably with our knowledge of the activity of estrogenic hormones in physiologic conditions. (1) The occurrence of the peak of estrin concentration in the blood during the early part of the second half of the normal menstrual cycle would seem to be associated with ovulation. This observation is in keeping with the incidence of ovulation at the time of estrus, which in the lower animals is the climax of estrin effects. (2) The intensity of spontaneous rhythmic contractions of excised human fallopian tubes apparently follows that of this estrin curve, since Snyder and Seekinger¹⁹ found the greatest activity in the middle of the interval. (3) The studies of Allen and others²⁰ on the estrin

content of human ovarian tissues gave results definitely related to the blood estrin curves, and although the amount of hormone present in the ovary is not necessarily a true index of the total produced by that organ, the concomitant findings are at least very suggestive. They obtained high yields of the hormone from recent corpora lutea removed on the thirteenth to the seventeenth day of the menstrual cycle, and there was a considerable decrease by the twentieth to the twenty-second day. (4) A characteristic of the menstrual cycle of monkeys, which is pronounced in baboons and chimpanzees (Zuckerman²¹), is a swelling and deep reddish discoloration of the skin of the external genitalia. This is an estrin effect, and it reaches its maximum intensity at about the middle of the cycle or near the time of ovulation. (5) And finally, it has been shown throughout this report that the blood findings are definitely comparable with the results obtained from the study of the daily estrin concentration in the urine.

It is impossible at the present time to properly interpret the significance of the presence of estrogenic substances in the blood of women. These hormones have been considered as ovarian in origin, and the cyclic increase and decrease which occurs during the course of the menstrual cycle points to a close association with follicular activity. Their appearance in the blood of preadolescents at the time that the secondary sexual characteristics begin to develop is also in favor of a gonadal source. On the other hand, the occurrence of estrin in the blood and urine of castrates and of women in the postmenstrual period is a conclusive demonstration that it must have an extraovarian origin. As Zondek¹⁰ has shown, it does not seem likely that an amount of the hormone sufficient to give the blood and urinary findings which have been reported comes from the ingestion of food containing estrin. In any case, the incidence of estrin in the blood in association with involutional changes in the uterus and vagina shows that in these individuals it does not exert the same hormonal activity which is manifested in the presence of functioning ovarian tissue. The question must remain *sub judice* for the present, but the solution may come from further chemical studies on the nature of the estrogenic substances present in the blood and urine.

SUMMARY

1. The technique of the mucification test for the demonstration of estrogenic substances in blood is described, with a few modifications.
2. The examination by this method of solutions containing known amounts of theelin at various dose levels showed a high degree of accuracy.
3. The present report is based on the examination of 401 specimens of blood from 84 women and 15 prepubertal girls.

4. The blood of 5 out of 7 normal girls between the ages of eight and ten years gave positive reactions for estrin, whereas the tests were negative in 7 out of 8 girls from four to seven years of age.

5. In 22 out of 25 patients it was found that during the course of the menstrual cycle there was an increase in the concentration of estrin in the blood, which occurred during the midinterval and seemed to be associated with ovulation. A secondary rise just before or at the onset of menstruation was noted in seven instances.

6. No characteristic variations were observed in 4 patients with anovulatory cycles.

7. In 10 out of 16 cases of menorrhagia, polymenorrhea, or uterine hemorrhage due to hyperplasia endometrii, a rise in the concentration of the blood estrin was observed at the onset of the bleeding.

8. Three types of blood estrin curves were found in patients with amenorrhea. (1) There was a cyclic rise and fall in the amount of estrin. (2) A constant moderate amount of estrin was present. (3) There was a persistent absence of demonstrable estrogenic hormone.

9. Estrogenic substances were found in the blood of women following castration and in the postclimacteric period.

10. The presence of estrin in the blood was demonstrated in association with increased amounts of anterior pituitary sex hormone.

This work was supported in part by a grant from the Rockefeller Fluid Research Fund of Stanford University School of Medicine.

My thanks are due the members of the Pediatrics Department for obtaining specimens of blood from the prepubertal girls; to Dr. G. F. Jones, Dr. K. M. Murphy, and Dr. L. M. Bayer for their cooperation in the study of the patients; and to Mr. John J. Kan and Mr. Pierre Lassegues for their technical assistance in conducting the tests.

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DISCUSSION

DR. OTTO H. SCHWARZ, St. Louis, Mo.—My associate, Dr. Soule, has been very much interested in the separation of the hormones in the blood of the human being. I shall read from his notes.

"We have utilized Dr. Fluhmann's method for studying the presence of estrogenic hormones since the spring of 1935. At this time we should like to discuss the problem of the passage of hormones across physiologic barriers.

"The question of the presence of hormones in the fetal circulation has been a problem of extensive study. Various investigators have demonstrated that adrenalin, insulin, posterior-lobe pituitary, and parathyroid hormones are *not* transmitted through the placenta. Schlossman (1932) discussed the entire problem of interchange of substances between mother and fetus through the placenta.

"With regard to the sex hormones, we have demonstrated that the anterior-pituitary or anterior-pituitary-like hormone which is responsible for the "positive" Aschheim-Zondek or Friedman test is *not* present in the human cerebrospinal fluid. More recently, by utilizing this same "rabbit" test, we demonstrated that this pituitary or pituitary-like factor is not transported through the human placenta. This was shown by performing rabbit tests on maternal blood serum and fetal cord blood serum. These specimens were taken simultaneously at the time of delivery and the tests carried out in the routine manner. In *no* case were we able to demonstrate "blutpunkte" with cord blood serum even though we used two or three times as much cord blood serum as maternal serum. The obvious conclusion is that this anterior-pituitary or pituitary-like hormone does *not* pass the placental barrier.

"Various methods for the demonstration of estrogenic hormones have been tried by many observers. In most instances these techniques have either proved wanting in accuracy, too complex, or not sufficiently consistent.

"So far as the demonstration of estrogenic hormones in the maternal and fetal circulations is concerned, the literature is rather sparse. Schlossman quotes several authors and concluded that folliculin is present in the fetal as well as in the maternal circulations. He does not attempt to answer the question as to whether it is present as a substance transported through the placenta or whether it is a product of the placenta itself. Skowron and Skarzynski concluded that in rabbits the follicular hormone passes through the placenta.

"By using Fluhmann's method for the study of estrogenic hormones as originally described in 1934, we continued our study of the interchange of hormones through the placenta. Fetal cord blood and maternal blood taken simultaneously were tested by this method. Various dilutions of these serums from full strength to 1:20 were tested and in all tests it was found that these hormones gave the *same* degree of reaction in both maternal and fetal samples. This is a most interesting observation in view of the knowledge that other hormones are not transported across the physiologic barrier.

"We have also used Dr. Fluhmann's method for the study of various endocrine problems, particularly the menopause state and various amenorrheas. Our present approach is to make a blood study by this technique and a parallel study of an endometrial specimen *and* the vaginal mucous membrane. The data concerning this work is as yet not ready to be reported."

DR. EMIL NOVAK, BALTIMORE, MD.—In Dr. Fluhmann's interesting study, some of the results he reports clarify our clinical and histologic impressions, while others are rather confusing. The finding of estrin in prepubertal phases is in line with the results of others, and also with the fact that follicle development occurs long before the age of puberty. In amenorrhea one may find a very trophic endometrium, or one may find, as we have done in a few cases, an endometrium which apparently passes through a cycle identical with that of the normally menstruating woman except for the bleeding phase. Just what replaces the latter is an interesting problem which remains to be worked out, although it should not be a difficult one in view of the present-day use of the endometrial biopsy.

I was much interested, too, in Dr. Fluhmann's frequent finding of estrin in women after the menopause or after castration, an observation which likewise conforms to the findings of others. It also fits in with the fact that proliferative endometria, and even hyperplasia, may be found in elderly women long after the menopause, an observation upon which I hope to elaborate in my own paper tomorrow. I have been more and more impressed with the fact that the term "senile endometrium" is only a chronologic one, for it may include not only the atrophic type, but also pictures indicating all degrees of proliferative activity, presumably as the result of an estrogenic stimulation of some sort, though we do not know its source.

DR. SAMUEL H. GEIST, NEW YORK, N. Y.—In order to correct an impression that one may possibly have received from what Fluhmann said, I wish to point out that Frank's results do not differ so very much from those of Fluhmann as determined by his new method. The mucification of the vagina was first regarded as a specific effect of the corpus luteum. Later it was ascribed to injection of estrogenic substances. As we now know, there are probably a number of estrogenic factors in the organism, either in free or combined form. It is quite possible that the mucification reaction is influenced by one or the other of these factors to a greater degree than the vaginal smear reaction. This may account for some discrepancies between the results obtained by the Frank and the Fluhmann reaction.

In a series of amenorrhea cases, some primary and some secondary, the same picture was obtained as Fluhmann showed in his slides. There were certain individuals who showed a very low level of hormone, whereas others showed a definite cycle. In those cases that were associated with bleeding and shortened intervals, the same picture was obtained in many of Frank's cases where just before the onset of the bleeding, or while the bleeding was in progress, a greatly increased amount was present in the urine but none or only small amounts in the blood. In the menopause cases, in spite of very active menopause symptoms, some women show a considerable amount of estrogenic hormone in the blood and urine. In addition the biopsy investigation of the vaginal mucosa was more or less in conformity with the hormone excretion. Some of the cases that had symptoms and excreted hormone still showed perfectly normal vaginal mucosa. There is therefore not so great a difference or contradiction between Frank's work and that just reported, as one might have gathered from Dr. Fluhmann's remarks.

DR. FLUHMANN (closing).—I did not wish to give the impression that all of my results were contradictory to those reported by Frank. What I had chiefly in mind was Frank's finding that estrin rises in the blood from three to seven days before normal menstruation, whereas in my studies this rise seems related to ovulation rather than menstruation. It should also be said that it is not right to speak of a "contradiction," because the estrin determinations in the two investigations were made by widely different methods.

It is a temptation to speak in more detail of the clinical aspects of this work, but at this time it would be hazardous to do so. However, I should like to refer to its application to our present concept of the cause of menstruation. As you know, Allen's "estrin-deprivation" theory seeks to explain the occurrence of uterine hemorrhage as due, not to a direct action on the uterine mucosa, but to the removal of ovarian influence following its stimulation of endometrial growth. From my studies with blood-estrin determinations it appears that uterine bleeding may take place at a time when there is a high amount of estrogenic substances in the blood and conversely a rise and fall of the hormone content may be associated with amenorrhea. These results may be open to several interpretations, but it at any rate seems probable that estrin-deprivation *alone* is not sufficient to account for the occurrence of menstruation, and other factors must also play a part in the normal menstrual cycle.

TOTAL VERSUS SUBTOTAL HYSTERECTOMY

A CLINICAL AND TECHNICAL STUDY

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THIS is merely an expression of opinion based upon personal experience arising out of 550 consecutive cases of hysterectomy, about equally divided into the two categories. The two series are as alike as possible in every circumstance and antecedent. In the first half of the series, the subtotals markedly preponderate. As my experience and finesse improved, the totals greatly outnumbered the subtotals, so that for the past year, the total hysterectomies constitute about 90 per cent of all my hysterectomies. The uterine pathology included all the common diseases. Many were complicated by appendage troubles of almost every variety. The uterine preponderant diseases were fibroids, fibrosis, corporeal malignancy, advanced cervical disease, chiefly in the third and fourth decades, and states of pelvic allergy associated with uncontrollable uterine hemorrhage. There were only five cases of cervical cancer, after treatment by radium, in which hysterectomy was deemed advisable.

I wish to state most emphatically that it is farthest from my intention to force the unskilled gynecologic surgeon into an operation, graver than that for which he is fitted by experience. But to the skillful surgeon, to whom a slightly longer operation presents no greater deterrent than the extra time that is expended, the total hysterectomy, *ceteris paribus*, will present great advantages to the patient, as well as great surgical satisfaction.

There are advantages and disadvantages to each of the two types of hysterectomy.

The disadvantages of total hysterectomy are:

1. Greater time expended at operation.
2. Greater skill required.
3. Greater blood loss.
4. Greater danger to vital organs.
5. Greater difficulty if the pelvic organs are fixed deeply in the pelvic cavity, or if patients are obese.

The advantages of total hysterectomy are:

1. Fewer immediate postoperative complications.
2. Fewer remote sequelae.
3. Smoother recoveries.

The disadvantages require no further elucidation. I believe they will receive general acceptance. On the other hand, the advantages may require considerable discussion.

The average difference between a subtotal and total hysterectomy is between five and fifteen minutes, a negligible factor in the average case. The skill required is merely that derived from experience, preferably primarily derived from one who has perfected the technique, with an accurate knowledge of the relative and absolute proximity of the vital pelvic structures, and care in avoiding undue tension upon tissues. Tension is one of the greatest deterrents to forming union, and one of the most frequent causes of postoperative pain. The great onus of care in these cases surrounds the invisible ureters. To some they become a mental bogey. A ureteral complex, you will excuse the term, is one of the worst of emotional acquisitions in the surgeon. Some men seem to be unable to avoid them, and their mental stress to go wide of them seems to act like a lodestone.

To the best of my knowledge, I have never injured a ureter or bladder in hysterectomy. That does not mean that it has not happened, but merely, if it did, it was not only unobtrusive, but not even recognizable when sought. Operative bladder injuries are rarer than ureteral complications, in the experience of the general run of gynecologic surgeons. It is my experience that it is extremely difficult to injure the bladder when it is empty and contracted. It is one of the most elusive organs.

The difference in the blood loss in the two types of operation may be negligible. In the ordinary run of cases it is so. But it can be considerable, especially in hemorrhagic cases, or when a clamp or suture fails in its requirements. A word of caution here may not be amiss. A careful preoperative inquiry into the patient's history, as to untimely or copious uterine hemorrhages, nosebleeds, migraine, and familial history of vascular instabilities, may make one cautious in carefully suturing raw surfaces completely, and insisting upon a most thorough hemostasis. Where the history is at all suggestive of a hemorrhagic state, the usefulness of a preoperative blood transfusion and a repetition of the same on the seventh day after surgical intervention will obviate the serious oozing at operation, and prevent late postoperative bleeding. It is a singular fact that vascular unstables are prone to develop an advanced state of hemorrhagic tendency about the eighth day. This, though frequently occurring as an expression of a low state of sepsis, is also a sequel of low platelet count at that period, and, in most cases, can be forestalled by a carefully matched transfusion. These cases should be matched for three-quarters of an hour, and any abnormality should be guarded against. These nonseptic hemorrhagic cases are prone to develop wheals at the point of any hypodermic injection, and other signs of skin irritability. A special paper is being devoted to this important subject. Should the secondary hemorrhage be due to sepsis, it will occur

usually between the eighth and twelfth day after operation. The sepsis is frequently ignored, because the temperature seldom rises more than a fraction above 99° F. and is usually continued over several days. It is in just these types of septic cases that either blood or vessel, or both, becomes so altered by the bacterial toxin, that diapedesis or rhexis occurs. Hemorrhagic states, as previously stated in my monograph on puerperal infections, rarely occur in acutely septic cases, but are most common in the continued cumulative low-grade infections, which do not rouse the body to the formation of antigens. When vaginal hemorrhage occurs, and it has occurred in my series of total hysterectomies in 2.25 per cent of cases, it has always been in these two types of cases: the vascular unstables, both septic and nonseptic; the vagina should at once be cleared of clots and packed gently with gauze with an uterine packer. To leave the vagina filled with clots is tantamount to inviting further bleeding. In every instance, this procedure, preceded by a transfusion, has promptly arrested the bleeding.

Generally speaking, total hysterectomy is easier in the parous than in the nulliparous, due to the greater mobility of the uterus, owing to the lengthening of its ligaments. Low set, fixed uteri may present unusually difficult surgical circumstances. Particularly is this so in cases of subacute or chronic pelvic inflammatory disease. But the difficulty, when overcome, brings a sense of great satisfaction, for it is in just these types of cases that it pays to remove the cervix with its susceptible mucosa.

About 70 per cent of patients who have total hysterectomies void spontaneously after operation, as against 45 per cent of subtotals. This circumstance, confirmed by all my house surgeons in the four different hospitals, seems contrary to all the laws of probability. An explanation has been sought, but nothing satisfying has been forthcoming. Is it that in the subtotal only, certain branches of the autonomic nervous system are severed, and that others are thereby thrown out of normal function; whereas, in the total hysterectomies, the majority, if not all, of the autonomic nervous system to the bladder is severed, causing the bladder, therefore, to become an automaton without sympathetic nervous control? In our present imperfect knowledge of autonomic vesical control and autonomic vesical distribution, it is quite impossible to vouchsafe anything but theories. Consult any work upon the results of section of the sympathetics upon vesical control, and one is led into a perfect orgy of contradictions and confirmations among the experimenters. The low percentage of spontaneous bladder evacuations in subtotals has been explained, by one of my colleagues, upon the basis of an inflammation spreading from the retained cervical stump to the bladder, an explanation that seems quite inadequate for many valid reasons.

Primary hemorrhage has never occurred in any one of the 550 cases, so that in this respect they are equal. Thrombophlebitis is a much more

common complication in subtotal hysterectomies. The comparison is most striking. The percentage was three to one.

In all clean cases, thrombophlebitis may be taken as an index of a man's technic, both in obstetrics and in gynecology. Let this be most emphatically stated. So many, whether from ignorance or self-deception, assume that thrombophlebitis is an unpreventable misfortune, quite beyond their control. There is a ready explanation for the preponderance of thrombophlebitis in subtotals. It is to be found in the cervical mucosa. Just a few lines about pelvic thrombophlebitis. It is rarely diagnosable, except in its secondary complications. It is rarely acute, and most dangerous when of low-grade infection, or in its defervescence after an acute or subacute attack. The general agent of thrombophlebitis is an infection of low virulence and in the vast majority of cases it emanates from a mucosal disease. In this respect, the mucosa of the cervix fills all the requirements. Hence the relatively higher percentage of thrombophlebitis in subtotals, as against totals. The aseptic technic in both operations in my series was essentially the same, so the higher percentage must have been due to an agent residing in the tissues. And now, when upon the subject, it may be opportune to stress something which has not received sufficient attention: inflammatory diseases run very different courses, depending upon the tissues in which they are placed. Infections in mesoblastic and ectodermal tissues usually run a purely local and rapidly conclusive course, or a virulent and rapidly critical stage with an equally rapid cure. Restoration to normal function is usually complete in proportion to the rapidity of the disease, provided the patient survives the storm. In mucosal diseases, however, the great majority are subacute or chronic from their inception. Those that are not tend to become so eventually, and the tendency for the disease to linger indefinitely is the rule. This tendency leads eventually to two distinct changes, hyperplasia or hyperfunction, or both. The virulence dies down, and the corporeal reaction is then seldom sufficiently active to effect a complete cure. Thrombophlebitides are preponderantly mucosal in origin. In the cervical mucosa we have a classical example of these changes, and the organisms of the cervix are ready, in their attenuated form, to become the active agents of thrombophlebitis. That these organisms are still markedly pathogenetic can be clearly shown by the frequent incidence of secondary septic hemorrhage, when cervical amputations and suchlike operations were the vogue. Many of us in those years saw women, ostensibly in the bloom of health, submit themselves to cervical operations, only to be found on the 8th to the 12th day almost at the point of death, through septic hemorrhage. Why? Because we amputated through diseased mucosa. Why the delay to the twelfth day? Because the organism was semivirulent. Many of these cases developed pelvic thrombophlebitis and succumbed to its accidents. Mucosal disease is one of the greatest

menaces to primary union. Can this mucosal menace be removed by cautery? That depends. In many cases, the disease is limited to the mucosa proper, an endocervitis. In others, the organism is invasive, causing a large, hard, cystic cervix, a cervicitis. In still others, there may be combination of both.

In cases of simple endocervicitis, coning out the cervix and cauterizing the residual portion of the canal may be effective. In the cervicitis types, cauterization, except it be very deep and destructive, is more harmful than no cauterization at all. The ideal remedy is total removal, when the skill and experience overbalance the risk.

Drainage was not used at all in any of the cases, and complete closure is a fixture.

Subtotal hysterectomy is often disappointing in its late sequelae. In a goodly percentage of my cases a leucorrhea developed, which did not exist prior to operation. In many cases, endocervicitis and ectropion developed after operation, necessitating treatment. This invariably leads to disappointment in the efficiency of operation. Both the above changes, I believe, can be attributed to the abnormal status of the cervix. Doubtless, in subtotal operations, the cervix must suffer changes in nutrition and nervous impulses, which eventually lead to a state of pathology.

That these abnormal changes are in part dependent upon the menstrual flux is shown by the infrequency of these abnormal developments when both ovaries are removed with the body of the uterus. In five of my patients, there were very troublesome cervical hemorrhages, that came on some months after subtotal hysterectomy. Four of these were operated upon for continuous metrorrhagia, that resisted every form of treatment; none of them showed any appreciable pelvic pathology, either by bimanual examination, or at the time of operation. Two of them had two sterilizing series of deep x-ray, with recurrence of hemorrhages after a period of amenorrhea. One had radium once, and three series of deep x-ray in doses estimated sufficient to sterilize, at least temporarily, if not permanently. It is my practice to cone out the cervix in all subtotals, and I feel very confident that no endometrium had remained, unless it had invaded the domain of the cervical mucosa. One is inclined to believe that, in some of these cases, vicarious menstruation is set up. This is a very logical conclusion, when one considers that the genital canal, from the fimbriated end to the hymen, is developed from a common "anlage," yet it exhibits four variations of epithelium, and four widely different functions. And when we consider that the endosalpinx, endometrium and vagina respond to the menstrual cycle, it would be extraordinary did not the cervix show a similarly periodic change.

In one such interesting case, a woman at 42 first came under my observation. She had had a subtotal hysterectomy for fibroids, five years previously. For the past

year she had regularly periodic discharges of blood, simulating menstruation, every three weeks. She was an intelligent English woman, who said that the blood was unlike menstruation in that it came on and stopped more slowly than normal menstruation. She came fearing cancer. Nothing abnormal could be found on examination. Operation for other causes had to be done, and the stump was removed at the same time. It showed no trace of pathology. It is necessary but to mention the incidence of carcinoma in the stump of a subtotal hysterectomy. The assurance to a patient that cancer of the uterus is an impossibility after total hysterectomy is a comfort to the patient in which the surgeon rightly shares. Cancer of uterus is a constantly recurring fear in the emotional life of every woman of post-maturity.

It is not a matter of indifference whether one allows the ovaries to remain. With their removal, the incidence of late cervical pathology is greatly reduced; the incidence of immediate and intermediate post-operative hemorrhage is reduced, especially in vascular unstables; and the late return of bleeding from the stump is practically unknown after total removal of the ovaries, except in cases of newgrowth. There is not the slightest doubt that ovulation, estrin and progesterin formation keep the tissues in the pelvis in a constant state of flux, with varying nutritional changes, rendering them much more susceptible to changes bordering upon, or invasive of, the domain of pathology.

My final plea is, if one's skill and experience warrant, if the case is a suitable one, a retrospect of cases shows that the total hysterectomy has much to commend it, above a subtotal. Where, on the other hand, the surgical risk, arising either in the surgeon or in the patient, would make the immediate risk the greater, then pursue the course that your conscience will dictate. But do not stop there, as regards the welfare of your prospective cases. Make yourself as proficient in the total as in the subtotal. It can be done. The mortality in this series is nil. The rest is in the lap of the gods.

TECHNIC OF TOTAL HYSTERECTOMY

The vagina is cleansed with sterile liquid green soap, and thoroughly dried. Care is exercised to empty the bladder completely.

Catgut, of the plain variety, chiefly Davis and Geck product, was used throughout. No. 2 was used for all major ligature purposes (never any larger size), and No. 1 for all peritoneal work. A minimum of catgut in each case was used. In over 90 per cent of cases, six No. 2 ligatures were sufficient. These were, ligation of the infundibulopelvic ligaments or the uteroovarian broad ligament, depending upon whether the appendages were to remain, or not. The next two ligatures are upon the lateral upturn of the uterine arteries, and the last two are upon the lower uterine branches, as far down as the fornices. The vault of the vagina is sutured continuously in two layers, with single No. 1, or No. 2, catgut as described later, and the peritoneum of the pelvic floor is united always by a single continuous No. 1 suture. Curved noncutting needles are used throughout, except when sewing the cervical stump in subtotal hysterectomy. I cannot overemphasize the importance of this little precaution. Round needles transfix. Cutting needles make a button-hole and cause much unnecessary bleeding.

OPERATION

The abdomen having been opened, the patient is placed in an exaggerated Trendelenburg position. The intestines are then packed off, and the pelvis explored. In the uncomplicated cases, one determines at once whether the appendages are to be removed or not. If these are to be removed, they are held up by the hand of an assistant or by the operator, and the broad ligament "*clear space*" is located. This is a space below the ovary, bounded internally and outwardly by the uterine vessels. It consists merely of two layers of peritoneum, without any appreci-

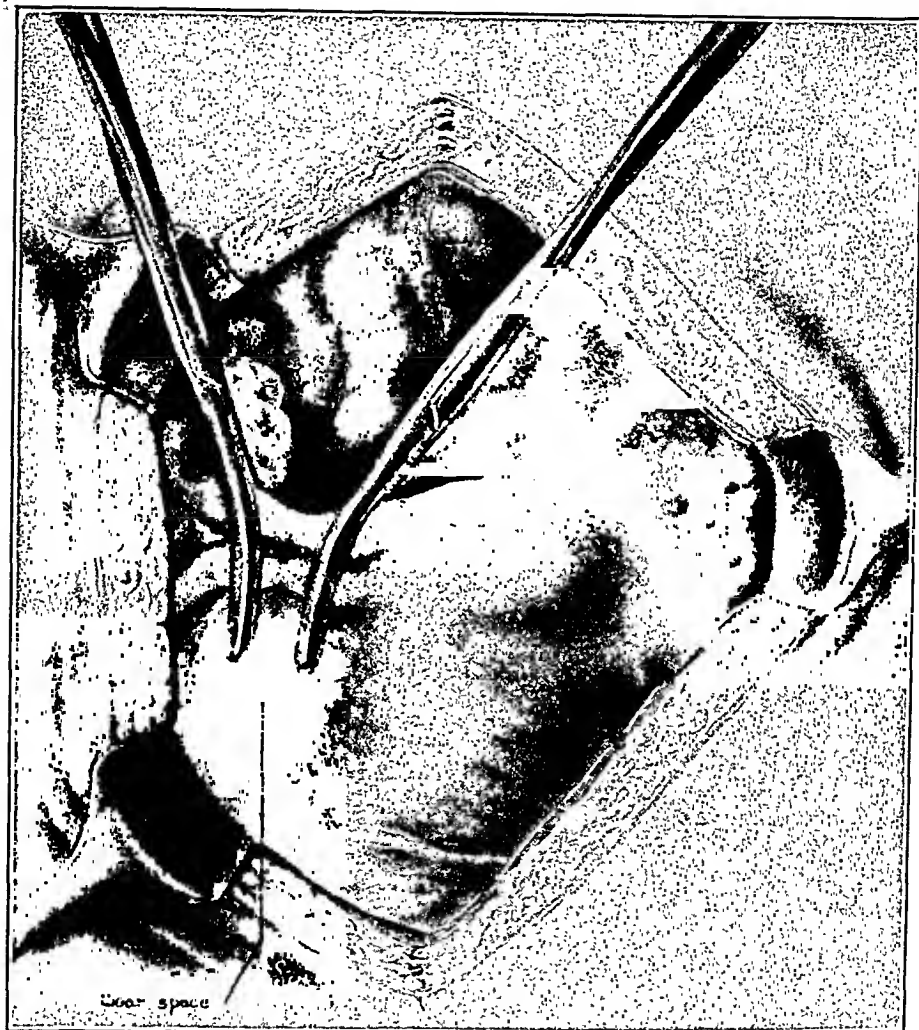


Fig. 1.

able tissues between them. If the finger impinges upon this area from behind, the digit will shine through anteriorly, or if the broad ligament is held up when tissues are lax, the space is translucent. A "Kelly" curved clamp (Fig. 1) is now placed upon the infundibulopelvic and round ligaments, having its tip in the clear space, and its convexity inward. A second and similar clamp is now placed upon the broad ligament between the ovary and uterus, with its tip juxtaposed to the tip of the first clamp. The appendages on that side are now completely isolated vascularily. In ordinary cases, the second clamp will include the proximal end of the tube, uteroovarian and round ligaments. This second clamp should be placed with its convexity outward. The appendages are now excised, being careful to leave at

least a quarter of an inch of tissue protruding through the forceps at the cut margin. This is to prevent slipping. The Kelly forceps should have longitudinal rugae along the whole blade, except at the tip, where they are corrugated, to prevent slipping.

The infundibulopelvic and round ligaments are now ligated by a figure of eight, which should transfix the round ligament, then through the "clear space," and again transfix the round ligament in the opposite direction. Ligation is then completed. The clamp should be released slowly as the ligature is tightened. I cannot

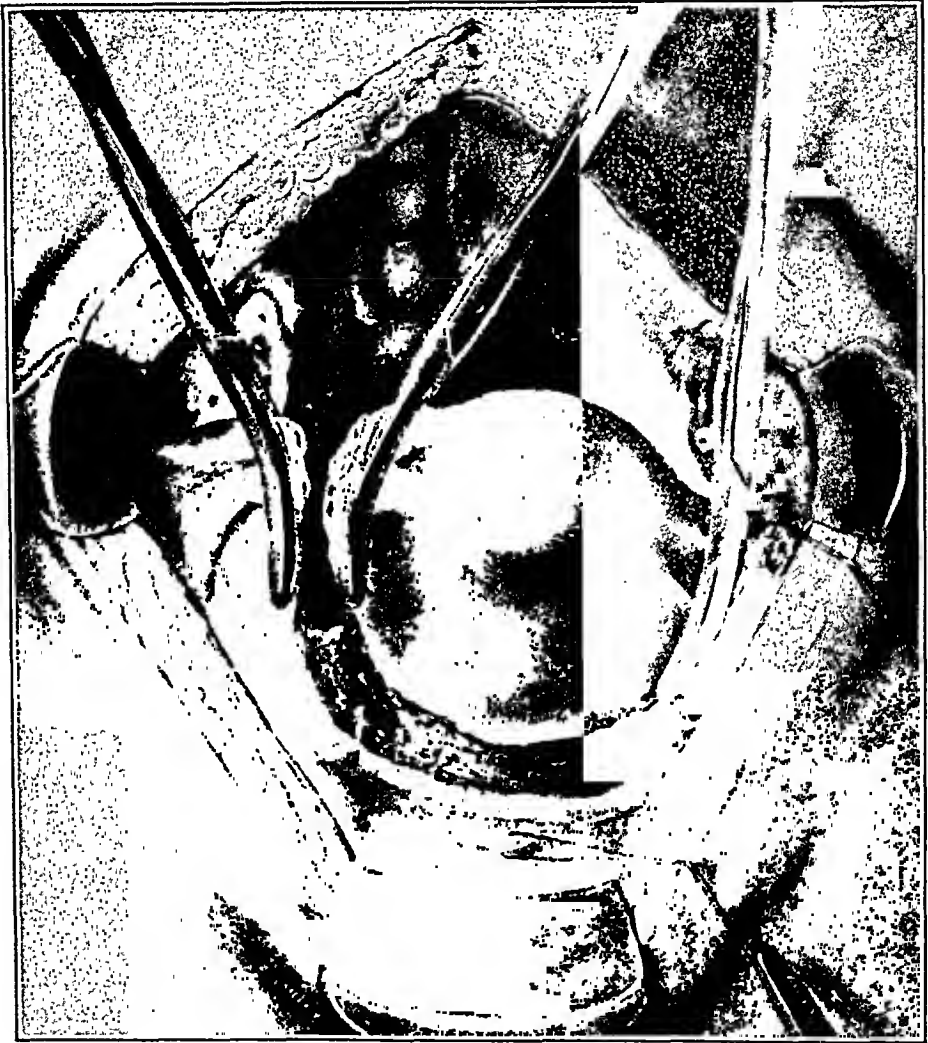


Fig. 2.

overemphasize the importance of this little procedure. Too quick release of the clamp, specially when dealing with the uterines, is inviting trouble, by allowing the tissues to escape from the grasp of the ligature.

The infundibulopelvic ligature is left long, and held by a forceps. On the opposite side the appendages are to remain. The "clear space" is again defined. The ovary and round ligament are pulled toward the pelvic wall and the first Kelly forceps is placed over the broad ligament, proximal to the ovary. Its tip should be in the center of the "clear space." Its convexity should be inward. A second is placed parallel to this, separated by one-third to one-half inch, with its convexity outward. These clamps include, in uncomplicated cases, tube, uteroovarian

and round ligament. Incision and ligation is now performed as described above, being careful to transfix the round ligament. There remain now but two Kelly clamps, which act as tractors upon the uterus. It is never necessary to grasp the uterus with volcels or any other form of tractor. These cause unnecessary loss of blood and tearing of tissue.

By its tractors the uterus is now pulled up and backward by the assistant, and the vesicouterine pouch exposed, by an anterior retractor. The anterior leaf of the peritoneum is now picked up on the left side at the vertex of the incision in the "clear space," and with a curved scissors, the peritoneum is incised in a curved

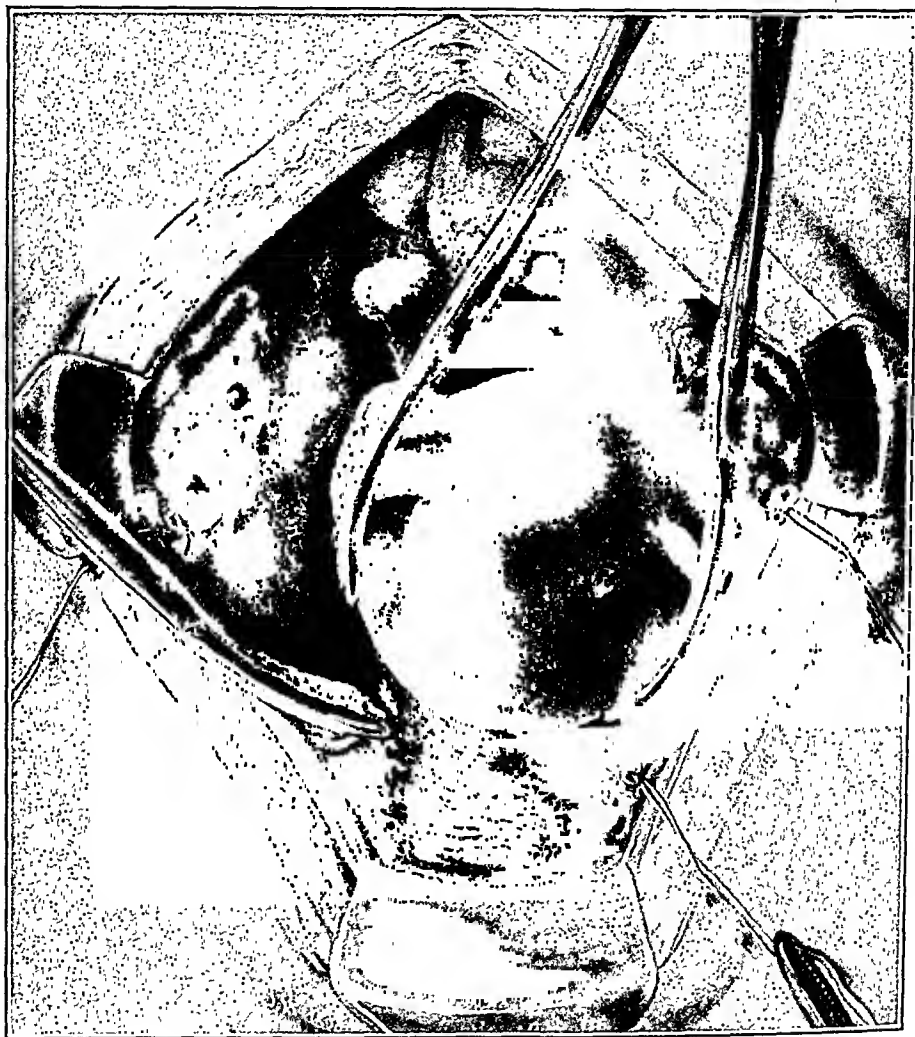


Fig. 3.

line in the vesicouterine peritoneal reflexion. The incision should end in the anterior leaf in the right "clear space." The operator now takes hold of the tractors with the left hand, and, with the index finger covered with one layer of sponge, the bladder is pushed down from the uterus and cervix. A No. 2 catgut now is made to transfix twice the bladder muscularis and vesical peritoneum (Fig. 2). This is not tied, merely held by an artery forceps. Traction is now put upon it by the second assistant, and a long special retractor measuring $2\frac{3}{4}$ by $4\frac{3}{4}$ is slipped below the reflected bladder, and the whole anterior wall of the uterus is now exposed. The uterus is again held by the operator and the separation of the bladder is now completed by the sponge-covered finger, down to the junction of the upper and middle

thirds of the vagina. An additional precaution lends a great deal of comfort. This consists in pushing the garnished finger well out on either side of the cervix and vagina, to separate the bladder from this region and to displace the ureters outwardly. A "Kocker" forceps with museux tip is now placed upon the upper uterine artery, at right angles to the uterine wall (Fig. 3). Its tip should impinge well into the uterine muscularis. Ordinarily it should be not less than $\frac{1}{2}$ inch and not more than one inch above the portio. This can be easily determined by a finger of one hand in the anterior, and another finger posterior to the vagina. A similar clamp is placed on the opposite uterine at the same height. The artery is now cut $\frac{1}{4}$ inch from the clamp margin on both sides. In cases of large uterine tumors, it is neater to place on each side, a second similar clamp $\frac{1}{2}$ inch above the first ones, to prevent a large escape of blood into the pelvic cavity. With a curved round needle the

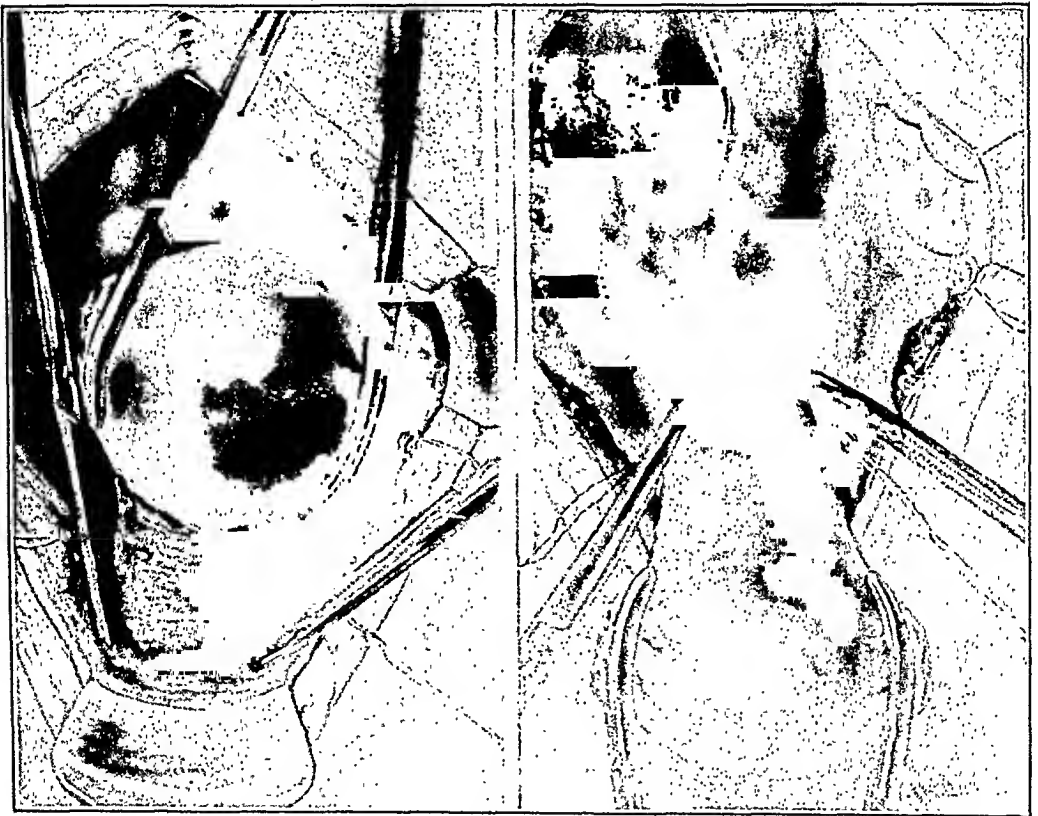


Fig. 4.

tissues are transfixed just below the forceps. The needle should not be driven through too close to the uterine wall, for reasons which will appear later. Ligation is now completed on both sides, and the clamps are removed.

The next step is securing the cervical branches of the uterines. Proceed as follows. First make sure that the bladder is clear, as above described, and held well out of the way of the cervix. Hemostasis should be complete. With the tractors pull the uterus up and out of the incision, and toward the symphysis, and expose the pouch of Douglas. Define the uterosacral ligaments (Fig. 4). Have your assistant pull the ligature on the upper uterine outward. Span the lower uterine with a "Kocker," placing the tip of the posterior blade mesial to the uterosacral of that side. Having made this impression posteriorly, turn your attention to the anterior blade. See that it is deep enough to go beyond the fornix. Then close it tightly on the cervix. Repeat the process on the opposite side. Care in placing these

clamps ensures safety to the ureters and bladder. The assistant now takes the handle of this forceps and draws outward and the operator cuts with a scissors boldly down the broad ligament, cutting always upon the cervix so as to leave one-fourth of an inch of tissue beyond the forceps on the cut side. The fact that you have reached the fornix is announced by a hollow sound quite different from that of the cervical tissues when severed by scissors. The process is repeated upon the other side of the cervix. When properly placed these last two straight clamps should converge at their points. The tissues uniting the lateral fornix to their broad ligaments are very loose and relatively bloodless, so that a portion of the lateral wall of the vagina can usually be freed, to equal that previously attained on the anterior wall. The assistant now holds the handle of the "Koecker" outward, the fornix of the vagina is now grasped with an "Allis" forceps on each side, the vagina is transfixed with a scalpel anteriorly, and the lower margin of the cut surface is caught with an Allis forceps. The circumcision of the vagina is now completed, above the two Allis forceps on the fornices (Fig. 5). The posterior vaginal wall is also grasped with a

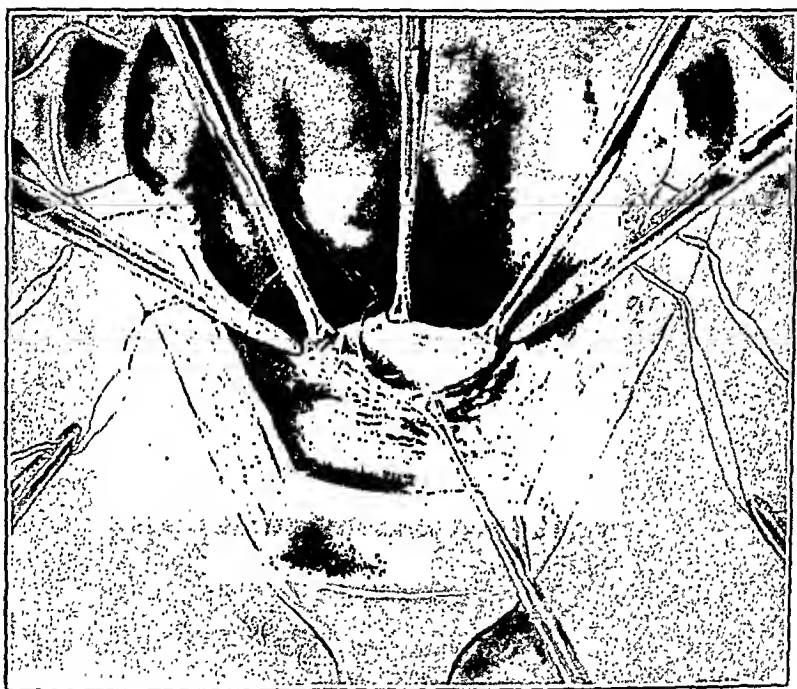


Fig. 5.

similar forceps. The vaginal vault is now defined by these four Allis forceps: one anterior, one posterior, two lateral. Any vessel in the paravaginal tissues (usually 'on the posterior wall) is caught within the grasp of an Allis. It is recommended that hemostat crushing forceps never be used where an Allis or other toothed non-crushing forceps will better serve the purpose.

It is never necessary to ligate the vaginal vessels. A continuous single No. 1 or No. 2 plain catgut (it should be long) is now used to close the vagina. One should begin at the patient's right, transfix from behind forward, and tie the first suture below and outside the Allis on the right lateral vault. The end should be held. Then continue across the vagina, being careful to close the left fornix completely. This suture should incorporate only the vaginal mucosa. Having reached the vicinity of the tip of the left Koecker, which still holds the lower uterines, the operator places a second layer over the vault, with the same continuous suture (Fig. 6). This should include posteriorly the intermediary tissues between the vaginal mucosa and peritoneum of the Douglas' pouch (including the latter, if so desired), and anteriorly

usually a well-defined cut layer of fascia between the base of the bladder and the vaginal wall. This is important in fixing the bladder from a sliding prolapse. The suturing should laterally stop short of the tips of the Kockers. The vault closure is now complete with the tying of the two ends of the continuous suture.



Fig. 6.



Fig. 7.

The lower uterines are now tied by transfixing the broad ligaments, just exterior to and slightly above the tip of the forceps, to insure that the ligature will remain distal to the forceps. The ligature is now looped and tightened down to the upper

margin of the tissue within the grasp of the forceps, as the handle of the Kocker is held toward the median line. The assistant now pulls the *handle* of the Kocker outward and the *tip* inward, and when so held, the operator tightens the suture, and, upon his dictum, the ligature is tightened synchronously as the assistant slowly releases the clamp. This ligature is inside the one previously placed upon the upper uterine. As a further precaution the ligature upon the lower uterines may now be tied over the ligature of the upper uterine ligature, in Staffordshire fashion. I have abandoned this method as unnecessary and productive of more knots for internal digestion.

Hemostasis should now be complete. The pelvic peritoneum is now closed as follows (Fig. 7). This is the most dangerous part of the operation. It is in this procedure that damage or ligation of the ureters most frequently occurs. I have catheterized the ureters in many cases, to demonstrate this. No. 1 single continuous is used. The posterior leaf of the clear space on the right is transfixed, then the suture is carried through the stump of the infundibulopelvic ligament (if appendages have been removed), or of the broad ligament (if appendages remain) internal to the primary ligature, and then it should pick up the layer of the anterior peritoneum beyond the round ligament. The assistant now pulls the ligature inwardly and one ties over the stump. The primary ligature and the single end of the continuous are now cut. One continues inwardly from right to left, closing posterior and anterior layers of peritoneum. As soon as one approaches the ligated uterines, one must proceed with greater caution. It is just here that the ureter emerges from among the uterine vessels and is covered only by a layer of peritoneum. Care should be taken that only peritoneum is included in the suture bite on the posterior wall. Once one has got past the right uterine ligature, one can proceed with impunity until the left uterine ligature is reached, where similar precaution is necessary. The left stump of the broad ligament or infundibulopelvic ligament is treated in a manner similar to the right. This line of suture draws the lateral supporting structures into a firm band of support in unison with the vaginal vault. The pelvic peritoneum has now been completely closed, and should be quite free from any exposed raw surface. Peritoneal toilet and closure of the abdominal wound complete the operation.

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Mankin, Z. W.: The Histogenesis of Endometriomata, Arch. f. Gynäk. 155: 671, 1935.

The author believes that all endometriomas arise from bits of normal endometrium which through one or another mechanism become loosened and are reimplanted elsewhere. He does not feel that they can ever arise from bits of degenerating cells during menstruation. Normal endometrium leaves the uterus and becomes secondarily implanted in one of three ways: first, through the tubal lumen, second, by direct transplantation during operations and third, by way of the uterine lymphatics. The first method results in those endometriomas which are serosal in location and are found on other abdominal organs and on the parietal peritoneum. The second method results in endometriomas of the scars in the abdominal wall, and the third method produces those tumors which are found in the ovaries, the broad ligaments, etc. These tumors can become implanted only during the period between puberty and the menopause. The author believes that all other theories which have been advanced to explain the development of endometriomas must be discarded.

RALPH A. REIS.

TOTAL HYSTERECTOMY BY THE ABDOMINAL VERSUS THE VAGINAL ROUTE IN BENIGN UTERINE DISEASE*

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COMPLETE mastery of a satisfactory technic for total removal of the uterus by both the abdominal and the vaginal routes is a minimum standard of operative skill that every gynecologist should exact of himself as early in his career as the circumstances of his period of apprenticeship will permit. Otherwise he will find himself frequently confronted with situations in which the best interests of his patients cannot be served because of his lack of proficiency in executing the operation that is best adapted to their needs. For, unfortunately, neither of these operations is best suited to all individuals requiring hysterectomy, and superlative skill in the performance of only one of them becomes but an exhibition of poor surgical judgment and mediocre ability when applied to the correction of pathology that could be better treated by employment of the other.

But, thanks to the collective efforts of an illustrious group of pioneers in pelvic surgery, rugged foundations were long ago laid down upon sound surgical principles that have stood the test of time upon which successive craftsmen have ingeniously fashioned the fine superstructures of present-day hysterectomy techniques, so that there is now available a sufficient number of perfected operative procedures for total removal of the uterus by both routes to satisfy even the most fastidious operator. Consequently, there no longer exists any legitimate excuse for failure to master at least one of each.

In a recent publication (*Am. J. Surg.* 28: 588, 1935), based upon a collective review of the literature on cervical stump cancer, I pointed out that subtotal hysterectomy is properly applicable to only four types of cases: (1) to those women requiring hysterectomy for benign disease who possess perfectly normal cervices; (2) to instances in which the operative hazard compels the execution of rapid and conservative surgery; (3) to a few cases where for good and sufficient reason it is of paramount importance to preserve the menstrual function; and (4) to most cases requiring hysterectomy during pregnancy. I also stated that because of the reprehensible prevalence of benign diseases of the uterine cervix, notwithstanding its many advantages, conservative subtotal hysterectomy has today only a limited field of application. Both in

*Also read by invitation before the Brooklyn Gynecological Society, Brooklyn, New York, December 6, 1935.

private practice and in clinic work it is the exception rather than the rule to encounter a normal cervix in conjunction with benign pathology of the uterine corpus requiring its ablation.

Now, if there is one fact more gratifyingly striking than the rest to be found in the recent literature upon total hysterectomy, it is that comparison of mortality statistics alone reveals practically no disparity between those who are wedded to the routine use of the abdominal operation and those who habitually employ the vaginal one. In both instances the immediate results obtained leave little to be desired and emphatically certify to the attainment of extraordinary surgical skill. But when a more inquisitive student undertakes to carry a comparison of results obtained with these two major operative procedures a bit further, he soon discovers that there is a woeful lack of recorded observations regarding the incidence of postoperative complications and duration of morbidity. And yet, certainly from the patient's point of view, such hazards as operative and postoperative hemorrhage, surgical shock, damage to bladder, ureters and rectum with consequent fistula formation, intestinal obstruction, cystitis, pelvic cellulitis, peritonitis, wound infections, phlebitis, thrombosis and embolism, pneumonia and the rest are realities to be specifically kept in mind while arriving at a decision as to which of the two operations under consideration offers the better guarantee of maximum success with minimum morbidity. For, let it be remembered that with the art of pelvic surgery so highly developed as it is today, there is scant ground for self-congratulation on the part of any gynecologist upon the mere attainment of a low operative mortality. The acid test of results obtained is applied through insistence upon unbiased follow-up observations continued not only during the period of hospitalization but also at intervals through later months, in order to determine the actual incidence of complications as well as the extent and duration of morbidity.

From such comparative studies one soon becomes impressed with the fact that in properly selected cases, a skillfully executed total hysterectomy by the vaginal route is a decidedly less formidable procedure as determined by its demonstrable effects upon the patient than is the same operation performed with equal finesse by the abdominal route. On the other hand, an attempt to broaden the scope of the vaginal operation beyond reasonable limits makes of it a mutilating procedure which serves only to discredit it and denotes neither sound judgment nor safe surgery. Obviously, it would be well-nigh impossible to lay down hard and fast rules that would infallibly govern one in the routine choice between these two plans of operative attack to which all pelvic surgeons would subscribe. Nevertheless, if at the outset of such an effort we fortify our contentions by setting up the premise that only those who have attained reasonable skill in the performance of both operations are qualified to offer constructive criticism, it should be possible to arrive at an agree-

ment both as to their relative merits and limitations. And so, with the hope of stimulating discussion that will ultimately achieve this end, I now venture to record certain convictions upon this subject arrived at only after deliberate contemplation of the teachings of others, coupled with and modified by my own observations and experience.

The following factors, it seems to me, are those that should govern the choice between the two operative methods:

1. *Age*.—Certainly no one will contest the assertion that major abdominal operations of any kind are not usually well borne by the aged and infirm. In this group abdominal panhysterectomy involves genuine hazard, whereas the vaginal removal of the uterus is astonishingly well tolerated. In middle-aged and younger individuals, while the difference is usually not quite as striking, there can be no question but that the immediate postoperative status of the average patient is distinctly better, the convalescence smoother, the incidence of minor complications diminished, and the period of morbidity shortened whenever the vaginal route can, with sound surgical judgment, be employed.

2. *Physical Status of the Patient*.—It cannot be too strongly emphasized that neither of these operations should be undertaken without a preliminary period of hospitalization sufficiently long to permit records to be made of a carefully taken history and complete physical examination, the latter to include, of course, such laboratory tests and other diagnostic aids as may be required to arrive at as accurate an estimate as possible of the individual's state of health and physical resources. Only strict adherence to this rule will safeguard the surgeon against the pitfalls of such surgical liabilities as obesity, severe grades of anemia, undernutrition, chronic exhaustion, and any one or more of a formidable list of constitutional and systemic diseases familiar to all of us. Discovery of the coexistence of any of these maladies with pelvic pathology that has prompted a patient to seek primarily the advice of a gynecologist imposes upon him the inescapable obligation to insist upon calling into consultation a competent medical colleague, in order that a comprehensive and intelligent plan of therapy may be evolved. Whereupon, it may appear that the contemplated pelvic operation had best be temporarily deferred or, perhaps, even abandoned altogether. If, however, it is deemed wise to include hysterectomy among the remedial measures agreed upon, it seems to me to admit of no argument that the restrictions thus imposed upon the surgeon compel him to employ the vaginal route whenever it is feasible to do so.

3. *Status of the Pelvic Floor and Supporting Structures*.—In nulliparous women whose intrapelvic ligamentous and fascial supports of the reproductive, vesical, and rectal units are normal and adequate, I always perform abdominal hysterectomy unless there exists some specific contraindication to its use. This, too, notwithstanding the fact that adequate

exposure for proper execution of the vaginal operation may always be had through use of liberal unilateral or bilateral Schuehardt's para-rectal incisions. However, the bleeding from these incisions is always copious and reconstruction of the divided structures so as to avoid permanent and unsightly deformity of the vaginal introitus is not always achieved. Moreover, even with the additional exposure obtained by this means the hysterectomy may still be difficult and hazardous in women with deep pelvis and strong, unyielding uterine supports. Complicated pelvic pathology, of course, tremendously increases the technical difficulties. Certainly, therefore, vaginal hysterectomy in the nullipara without uterine prolapse should be undertaken only by surgeons who have had large experience with this operation.

4. *Types of Pelvic Pathology to Be Dealt With.*—As a general rule, total hysterectomy by either route should not be undertaken if there exists acute or subacute infection anywhere within the boundaries of the operative field. The successful extension of present-day physical therapy to include even ambulatory dispensary patients is a commendable achievement, because it robs the time-honored argument which invokes the economic urge in justification of major pelvic surgery in the presence of active infection of most of its potency. There remains, nowadays, but scant excuse for subjecting any patient to this unnecessary surgical hazard. Someone has astutely suggested that if no elevation of temperature or of leucocyte count occurs following several vigorous bimanual examinations of the pelvic contents, one may safely conclude that the smouldering fires of lingering infection have become extinct.

Nevertheless, there often still remain, as the aftermath of the pelvic storm, extensive and dense adhesions involving not only the uterus and its adnexa but also the rectum, sigmoid, bladder, ureters, small bowel, and omentum. Usually, also, there is greatly diminished flexibility of the uterosacral and cardinal ligaments which offers strong resistance to downward traction applied to the cervix. Furthermore, the situation is likely to be complicated by the presence of cystic and adherent ovaries and bilateral hydrosalpinx. Under such circumstances I consider total hysterectomy by the abdominal route far preferable from every point of view.

Not uncommonly extensive pelvic endometriosis may closely simulate chronic pelvic inflammatory disease and cellulitis. A carefully taken history will often disclose a distinct and significant ebb and flow of regional pain intensity that coincides in a striking way with the several phases of the menstrual cycle reaching its maximum severity during the several days immediately preceding the flow. Moreover, such dysmenorrhea is frequently found to be of the acquired type, since the age incidence of this disease is predominantly after twenty-five. It is

commonly associated also with hyper- and polymenorrhea, although in many instances this is to be attributed to coexisting myomas or adenomyomas of the corpus uteri. Owing to the preponderance of endometrial implants at the bottom of the culdesae with subsequent extension to the anterior wall of the rectum and to the less common involvement of the bladder wall, symptoms referable to either of these organs and dominating the dysmenorrhea complex are particularly enlightening. In the last analysis, however, the diagnosis rests upon accurate interpretation of the findings upon vaginoabdominal and rectoabdominal palpation. There is a recognizable difference between cellulitis of infectious origin and infiltration occasioned by invading endometriosis, which is perceptible to anyone possessing a reasonably well-educated sense of touch. The difficulties of total hysterectomy may be greatly enhanced by extrauterine pelvic endometriosis. Each case must remain a law unto itself. In the majority of them I prefer the abdominal route, but if the major invasion has occurred in the rectovaginal septum, the vaginal route may offer worth-while advantages.

Again, when one encounters ovarian neoplasms in conjunction with the indications for total hysterectomy, it seems to me that both because of the vitally important matter of completing the ovariectomy without spilling any of the always uncertain contents of these tumors and because of the compelling indication in such cases to explore thoroughly the entire abdominal contents, laparotomy is obviously the route to be chosen. Preliminary evacuation of the contents of true neoplasms of the ovary is mentioned only to be condemned, except when the patient's condition compels its adoption as a last resort measure.

With regard to total hysterectomy for uncomplicated fibroid tumors associated with benign disease of the uterine cervix, several factors are to be considered before deciding upon the best method of operative attack. The most important of these are the size and the variety of the neoplasm. While it is unquestionably true that tumors as large, or even larger, than a four months' pregnancy may be successfully removed by the vaginal route, if morcellation is resorted to, the wiser course would seem to be employment of the abdominal route whenever the gross enlargement of the uterus exceeds in size an eight weeks' pregnancy. Caution should always be exercised in delivering through the detached vaginal vault even a tumor of this size because of the danger of serious damage to the base of the bladder and its sphincter muscle from overstretching. If intraligamentary, retroperitoneal, cervical, or subvesical fibromyomas are to be dealt with, one should always assume that normal anatomical relationships in the true pelvis have become distorted. Frequently this occurs to an extraordinary degree and failure to recognize the added operative hazards thus produced is responsible for many divided ureters and bladder punctures. In all such cases the abdominal route is obviously preferable. Nor should one

forget that pedunculated fibroid tumors of significant size are nearly always parasitic, obtaining much of their blood supply from adherent omentum, mesentery or gut, and that the separation of such adhesions even under direct vision through a laparotomy wound may be attended by considerable loss of blood. If there is no coexisting intrapelvic infection nor suspicion of malignancy in such cases, employment of the abdominal route permits use of autotransfusion throughout all stages of the operation preceding the final one of opening and detaching the vaginal vault. When one encounters extensive adnexal pathology complicating fibroid tumors, the abdominal route again is distinctly safer and easier of execution.

As pointed out under "Modification B" of my "Simplified Technique for Abdominal Panhysterectomy" published in 1929 (*Surg. Gynec. Obst.* 48: 248, 1929), if exposure of the cervix for the deeper dissection is rendered difficult by reason of the shape or size of a fibroid tumor, it is recommended that a subtotal hysterectomy at or above the level of the internal os first be done. Whereupon, the cervix may then be easily and speedily removed by use of the technique described. Obviously, this procedure should never be resorted to if there exists any suspicion of associated carcinoma of the cervical canal or of the corpus uteri. Fortunately, a preliminary diagnostic curettage affords an easy method for accurate determination of this question.

Total hysterectomy is frequently indicated in conjunction with the radical cure of various types of vaginal hernia, such as a large cystocele, rectocele, enterocele, and varying degrees of uterine prolapse, including complete procidentia. Some gynecologists advocate routine total hysterectomy as the preferential treatment of uterine prolapse and, until recently, I also subscribed to this view, basing my convictions upon the follow-up observations of private patients alone. However, in a recent statistical study of clinic cases operated upon in the Gynecological Department of the Johns Hopkins Hospital by a group of experienced men over a period of years, Everett (*Surg. Gynec. Obst.* 61: 403, 1935) found 30 per cent of recurrences after vaginal hysterectomy in prolapse cases as compared with only 4 per cent treated by the Watkins interposition operation. But whatever differences of opinion may exist regarding the best operative treatment of uterine prolapse, most gynecologists will agree, I think, that where total hysterectomy is indicated for other reasons in conjunction with correction of the various types of vaginal hernia, the lower approach is to be preferred.

5. *Association of Pelvic with Abdominal Disease.*—Only exceptional circumstances justify the performance of other major abdominal operations in conjunction with total hysterectomy. This is specifically true of elective gastrointestinal and biliary tract surgery. On the other hand, removal of a chronically involved vermiform appendix, or cure of an umbilical or ventral hernia may frequently be achieved in connec-

tion with abdominal hysterectomy and without added risk. Such procedures require, however, the exercise of sound and conservative surgical judgment.

6. *Associated Anorectal Pathology.*—Operative attack upon hemorrhoids, fissure and fistula-in-ano, rectovaginal fistula, and complete laceration of the perineum should not be combined with total hysterectomy by either route. If removal of the uterus must antedate correction of such maladies, my conviction is that subtotal hysterectomy by the abdominal route is far safer, because it evades the inherent danger of contaminating the operative field with subsequent development of serious, if not fatal, complications and also obviates the restrictions which such operations impose upon postoperative rectal therapy.

From this brief review of some of the major factors that should determine which of these two operations is best suited to the individual patient, it becomes evident that both of them have a wide range of usefulness and that under certain conditions each possesses distinct advantages over the other.

For the sake of emphasis, I have reserved for my concluding remarks a brief effort to focus attention upon one factor of safety common to both operations, the importance of which it would be difficult to exaggerate. Assuming that a preliminary critical and comprehensive diagnostic survey of the patient has wisely and judiciously accorded to the pelvic surgeon his proper place in the general therapeutic plan contemplated, and that the optimum time for the performance of total hysterectomy has been agreed upon between him and his medical colleague, this factor, perhaps more than any other, may determine the outcome of the operation as executed by either route both as regards mortality and morbidity. I refer to the degree of thoroughness with which the surgical toilet of the vulva, vagina, and cervix is carried out immediately preceding the operation. It is assumed, of course, that no surgeon would deliberately undertake a total hysterectomy by either route in the presence of any active infection of the vulva, Bartholin's glands, the urethra, the suburethral glands, or the cervix. But even in the absence of these obvious hazards, as many surgeons have learned from bitter experience, both the vaginal flora and the cervical glands may harbor the most virulent and dangerous types of streptococci, as well as other less formidable organisms. And there is abundant evidence to show that failure to recognize this fact is responsible for an occasional fatality and for many instances of postoperative wound infections, secondary hemorrhage, pelvic cellulitis, and other complications that contribute to a prolonged convalescence. Hence, the necessity for inflexible insistence not only upon extraordinary care being exercised in the surgical toilet employed but also that its application be delegated only to individuals sufficiently experienced to appreciate its importance.

DISCUSSION ON PAPERS BY DRS. GOODALL AND RICHARDSON

DR. HARVEY B. MATTHEWS, BROOKLYN, N. Y.—We can agree with practically everything that Dr. Goodall has said without argument. Our technic is not identical with his, but this is not important, for after all it is the operator and not the method that counts.

The number of supracervical hysterectomies compared to totals in Dr. Goodall's series were about equal. There was a time in our clinic, under the leadership of the late Dr. Polak, when we did more total than subtotal hysterectomies. In later years, however, after developing what we think is a good technic for the supracervical operation, we are now performing practically all supracervical. For example, in the last five years at the Long Island College Hospital there were 327 supracervical operations, and only 11 total hysterectomies. We lost one patient in the 327 of the subtotal group and one in the 11 of the total group.

In our clinic at the Long Island College Hospital, we employ the following routine in supracervical hysterectomy: The night before operation we insert a light vaginal pack of 4 per cent mercurochrome. At the Methodist Episcopal Hospital we have used 4 per cent mercurochrome in over 16,000 obstetric cases and have reduced our morbidity from 12 per cent to less than 5 per cent and therefore we believe it to be a first-rate germicide. On the other hand, any germicide may be used. At operation we thoroughly cauterize the cervix through the vagina from the external to the internal os. In doing the hysterectomy we "core out" from above down to and past where we have cauterized from below, following which cauterization from *above* is done. These procedures leave a "shell of cervix" that does not produce leucorrhea or backache. Furthermore, the likelihood of subsequent malignancy is cut to a minimum, not so much as in complete hysterectomy, for naturally if there is no cervix there can be no development of carcinoma in it.

Goodall did not mention infection this evening, but he speaks of it in his paper, a low-grade infection, associated with hemorrhage. We have seen such a low-grade infection and believe it is a condition that we have to contend with, more particularly in total hysterectomy. With the use of a preoperative germicide in the vagina, we believe that the likelihood of infection is tremendously reduced.

In his paper Goodall also spoke of removing or leaving the ovaries with reference to the behavior of the stump of the cervix that is left. There is no doubt that with no estrin or progestin being thrown into the circulation, the tissues are not in the state of flux that they would otherwise be, and consequently it seems important to remove the ovaries whenever the patient is thirty-five years or more of age.

The final decision between supracervical and total hysterectomy cannot be settled. We should ask ourselves whether it is better to perform subtotal hysterectomy with its limited morbidity and mortality rate, but with the likelihood of continued leucorrhea and backache and a greater tendency to malignancy, or a total hysterectomy with no leucorrhea and backache and no fear of malignancy but with a greater primary morbidity and mortality. These questions, I believe, have to be left to the individual surgeon. Much depends on the condition of the patient and on the ability of the operator to perform the operation of his selection.

DR. SIDNEY A. CHALFANT, PITTSBURGH, PA.—It has been our practice also to do supravaginal hysterectomies as a routine, limiting the complete hysterectomies to the carcinoma cases and to an occasional case where the cervix is badly diseased.

Our technic in the supravaginal hysterectomy is thorough cauterization of the cervix, and if all of the endocervical mucosa has not been entirely destroyed from below, to complete that from above by coning out the cervix. The presence of fibroids with old infection of the pelvis makes the complete hysterectomy quite difficult, and we have never felt sure enough of our ability to do panhysterectomy in such cases.

One disadvantage in panhysterectomy that has come to my attention recently in two patients operated upon in other clinics was a very marked shortening of the vagina. Both of these women were comparatively young.

Our technic in complete hysterectomy differs a little from Dr. Goodall's. We usually circumeise the cervix from below with a cautery. The dissection between the uterus and the bladder is thus facilitated very much. We open the anterior vault of the vagina, turn the cervix up and clamp from the base of the broad ligament on either side. It gives us practically two ligatures on either side and obviates the difficulty that sometimes occurs from bleeding from the cut edge of the vaginal vault. Following cauterization we have met an occasional case of bleeding about the eighth or tenth day when the slough separates. This has never been serious.

To be able to report 550 consecutive hysterectomies without mortality shows surgical judgment and operative skill of the highest degree, but I believe the average surgeon who does the bulk of the hysterectomies of the country will have as a rule a satisfactory result and will have a lower operative mortality by doing a subtotal hysterectomy.

DR. N. SPROAT HEANEY, CHICAGO, ILL.—I have had considerably more trouble with complete abdominal hysterectomies in their postoperative recovery than I have had with the supravaginal operation. I cannot imagine what factors could come into play to produce a postoperative hemorrhage following a supravaginal hysterectomy after the eighth day, providing there has been no cauterization of the cervix.

I agree with Dr. Richardson entirely as to the indications which he has laid down for the supravaginal, total abdominal, and the vaginal hysterectomy. We differ only in regard to those cases where no strict indications exist for a particular type of operation. In such cases he prefers to take them out supravaginally while I take them out vaginally.

Since the last report I have done 68 additional vaginal hysterectomies, making 695 since the introduction of ethylene into the Presbyterian Hospital. There were no deaths in these 68 additional cases, making the record 3 deaths in 695. In the 695 cases there was one case of thrombophlebitis. In none of the cases did I tie off a ureter.

When one has developed his technic in vaginal hysterectomy according to the indications laid down by Richardson until he has reached the point where he is satisfied with it, he then should select a case a little more difficult each time. It occasionally happens that he must have this skill for a particular case. For instance, an extremely obese young woman may have uncontrollable menorrhagia where a laparotomy on account of her obesity would be too hazardous to consider, leaving vaginal hysterectomy as the only logical operation. If unable to do this operation, the surgeon then would resort to radium in a case where ovarian function should really be retained.

It does not require a Schuehardt's incision to remove the uterus vaginally in a nulliparous woman, and I have never yet made such an incision. At most a small perineotomy is needed. In these last 68 cases 21 were nulliparous women.

I would like to emphasize that occasionally the removal of the cervix by the vaginal route and the body by the abdominal route is advantageous, particularly if the cervix should be badly infected.

DR. FLOYD E. KEENE, PHILADELPHIA, PA.—The choice between the vaginal and abdominal route in benign diseases of the uterus which requires total removal, is dependent upon several factors. First, the ease or the difficulty which the one or the other method affords in dealing with the diseased uterus, as well as the adnexal or intestinal pathology which may complicate the situation. No one can deny the superiority of the vaginal approach in the small myomatous uterus or in functional

bleeding when the vaginal outlet is sufficiently relaxed to permit of easy access to the field of operation. On the other hand, with a contracted vagina or with large tumors, abdominal hysterectomy can be performed more expeditiously; with less trauma to adjacent organs, less blood loss and more certain hemostasis. Certainly, the adequate exposure afforded by the abdominal route gives one more complete mastery of the situation in case inflammatory or neoplastic disease of the adnexa is encountered.

The second factor which must be considered is the mortality and morbidity incidence of each method. Reports by those particularly skilled in the performance of one or the other operation show a remarkably low mortality in both and what slight difference exists in the mortality rate is in favor of the vaginal method. As to the morbidity attending the two procedures, the absence of wound infection, the small incidence of phlebitis and lung complications make the immediate convalescence smoother in vaginal hysterectomy. I have seen no statistics dealing with the ultimate results, but from personal observation I have found no superiority of the one over the other.

Finally, the skill of the operator plays an extremely important rôle. I agree in principle with Richardson that the gynecologist should be equally skilled in both methods, but the truth of the matter is that in practice this does not apply to many of us. Had I the skill of Sproat Heaney in the performance of vaginal hysterectomy, I, too, would be its ardent advocate; lacking this, I shall continue to favor the total hysterectomy of Richardson which has given excellent results. I represent a clinic in which vaginal hysterectomy has never been a popular procedure, and we can be criticized justly for not using it more frequently. However, extending the indications for the vaginal approach to include lesions which can be handled more satisfactorily by the abdominal route is also to be criticized.

DR. JAMES C. MASSON, ROCHESTER, MINN.—We must realize that there is a legitimate field for the three types of operation and definite special indications for each one of them. I am satisfied that any gynecologist who is doing much surgery can do any one of these operations with almost an equal mortality and morbidity.

The ordinary surgeon who is not specializing in pelvic diseases is inclined to overlook the value of vaginal hysterectomies, especially in cases of slight prolapse associated with a cystocele. In spite of what one of the essayists said, I believe the cystocele can be more satisfactorily taken care of by the vaginal route.

I feel that the subtotal operation should be done in young women who are still in the active menstrual period. It is important to save some of the cervix, and in some cases it is advisable also to save some of the endometrium above the internal os. In the great majority of cases, in women at the menopause or later, especially if they have had children, the total operation is the one of choice and in the hands of any one who is doing much pelvic surgery it can be done as safely and with less morbidity than the incomplete operation.

Our statistical department has given me some statistics on these operations, covering ten years from 1925 to 1934 inclusive. There were 2,085 total hysterectomies for benign conditions, with a mortality of 1.5 per cent. There were 2,002 subtotal hysterectomies for benign conditions, with a mortality of 1.4 per cent. There were 834 vaginal hysterectomies for benign conditions with a mortality of 1.7 per cent. The vaginal hysterectomies were done, I must admit, on bad surgical risks, many being elderly and many stout people. I do not think, however, that the stoutness alone should interfere with the abdominal operation if the patient is in good surgical condition. These patients seem to stand the operation very well if it is not too prolonged.

In regard to removal of the cervix and the danger of cancer, I do not feel that the cervix that is left has any increased danger of becoming malignant, yet in the

clinic where I work we have seen more than 100 cases of epithelioma of the cervix. There have been over 500 cases altogether that came to the clinic complaining of some trouble in the cervix following subtotal abdominal hysterectomy, the great majority of them having had no trouble in the cervix before operation. In about half of these cases there was enough trouble so that it was thought advisable to remove the cervix. These are the combined results of eleven operators.

DR. LILIAN K. P. FARRAR, NEW YORK, N. Y.—After reading in the preliminary report of this meeting the titles of the two last papers, I looked up the records in the Woman's Hospital for hysterectomies done in the past twenty years.

YEAR	VAGINAL	SUPRAVAGINAL	COMPLETE
1916-1925	321	2,267	619 (Incl. Wertheims operation)
1926-1930	152	1,218	255
1931-1935	245	1,217	398
Total	718—2.7 %	4,702—3.04%	1,272—4.24%
Grand total	6,692—3.23%		(Without Wertheims, 3.3%)

The above table shows the mortality for all hysterectomies done by the attending staff including those done by the internes in the Woman's Hospital in the years from Jan. 1, 1916, to Dec. 31, 1935. There were several Wertheim operations in the total hysterectomies, and if we deduct these deaths, the mortality for the total hysterectomies is 3.3 per cent or a difference of only 0.3 per cent from the subtotal hysterectomies.

I am heartily in accord with Dr. Richardson in the limitations for the proper use of total hysterectomy, but I do believe that suitable cases can be operated upon by total hysterectomy by those specializing in pelvic surgery, who are willing to study the anatomy and technic, with as low a mortality as in the subtotal operation, or with even a lower mortality for it is certainly safer to remove the whole of a diseased organ than to cut into it and then leave a large portion in situ.

I have been interested to follow the admirable work that the American Board of Obstetrics and Gynecology is doing to develop young applicants. I only hope that they will include more anatomy in their requirements. I do not wish to minimize the importance of pathology, but it is seldom that the opinion of an expert pathologist is needed in a major operation, and a knowledge of pelvic anatomy is absolutely necessary at every step of an operation. I hope, too, that the time will come when the Board will be given the authority to supervise or lay down a course of instruction for internes who are specializing in obstetrics and gynecology, with instruction in anatomy and in technic, and perhaps to appoint someone to pass on the ability of an interne to use his hands before he has gone too far in the curriculum.

DR. WILLIAM C. DANFORTH, EVANSTON, ILL.—During the past few years in our service there have been about 550 abdominal hysterectomies, the majority of which have been done supravaginally. In this series there were two deaths, one of which was due to anesthesia. During the past four years we have used vaginal hysterectomy more liberally and in that length of time 170 cases have been done with no deaths. When we first began the frequent use of this operation we had two post-operative hemorrhages, neither of which was serious and both of which were easily controlled. In the last 100 cases no bleeding has occurred.

We do not use vaginal hysterectomy for the removal of large tumors or in dealing with cases in which pelvic inflammation has occurred or where extensive postoperative adhesions are feared. It seems appropriate that the gynecologist should use either method of approach and that he should be able to fit the operation to the patient.

In the hands of the average operator the mortality as shown by John G. Clark some years ago was about 5 per cent, far higher than that which is attained by expert pelvic surgeons, and the difference in the mortality of the two operations in average hands is probably greater, although there is little or no difference in the hands of the expert. In the average hands, therefore, subtotal operation is probably safest.

DR. JOHN A. McGLINN, PHILADELPHIA, PA.—In our last 100 cases there were 14 vaginal hysterectomies, by ligature, 9 vaginal hysterectomies by clamp, 3 total abdominal hysterectomies, and 74 subtotal abdominal hysterectomies. One of my group is to report, in the fall, 250 vaginal hysterectomies without a death.

We are very much the victims of our ancestors, and Philadelphia surgeons have never particularly favored the vaginal operation. It is only comparatively recently that I have done a vaginal hysterectomy in a way satisfactory to myself. But now that I am able to do all types of the operation I feel that I can select the operation which best fits the individual case.

Now do not let anybody criticize the vaginal hysterectomy with clamps on any academic basis unless they have had actual experience with the operation and have followed the convalescence of the patient for a year or two. I might say that since adopting vaginal hysterectomy with clamps we are operating upon women of forty years with endocrine bleeding, where we formerly used radium.

DR. GOODALL (closing).—I purposely did not deal with vaginal hysterectomy because this paper was a discussion between abdominal total and subtotal. The number of vaginal hysterectomies that I have done, I cannot give offhand, but they constitute quite a small percentage of the total hysterectomies done in the various hospitals.

RETROPERITONEAL PELVIC TUMORS ENCOUNTERED BY THE GYNECOLOGIST

JAMES RAGLAN MILLER, M.D., HARTFORD, CONN.

GYNECOLOGISTS from time to time are faced with the problem of differential diagnosis of a mass lying behind the peritoneum either in the true pelvis or in such proximity to the pelvic brim as to suggest its origin in the genital organs. Discussion in this paper is limited to nongenital tumefactions, lying behind the posterior peritoneum in and about the pelvis.

While it is usually possible before operation to reach a definite conclusion as to the retroperitoneal location of a tumor, only too often the exact nature and location are first disclosed after opening the abdomen in the course of a procedure which the operator thought to be a simple gynecologic maneuver.

It is possible also in most cases when the abdomen is open to make an accurate diagnosis by gross inspection or when in doubt to obtain a frozen section for immediate microscopic diagnosis. There are, however, certain masses which may not be biopsied without seriously impairing the patient's chances for ultimate and even for immediate recovery.

Such problems come but rarely even to the surgeon of large experience. When he meets the situation successfully, he is not likely to report the case unless it presents some unusual features such as enormous size, and if the patient does not survive, he is even less inclined to mention it. Many highly instructive lesions are thus lost from view, whereas much might be learned if they were properly classified and made available for study as a regional problem. One gains the impression on reading the literature that chapters in the various systems have been based largely on the reports of single types of cases viewed from the pathologic and not the regional point of view. Only in the systems of surgery and in the textbooks of pathology is the region, as such, considered.

The purpose of this paper is, therefore, to fix attention on the various possibilities which the narrowly trained specialist may encounter to his own discomfort. The case histories here reported are partly my own and partly those which have been made available by my associates.

1. URINARY TRACT

Anomalies of the upper urinary tract recently reviewed by Gutierrez¹ are usually suspected and diagnosed by well-known pyelographic methods. Silent lesions of the urinary tract, however, may be encountered during operation for fibroid uterus or tumor of the ovary. The possibility of solitary kidney must be borne in mind, also the fact that ectopic kidneys do not, merely because of their position, require treatment. If removal is necessary, one must remember that the blood supply of anomalous organs is usually anomalous. Thomas and Barton² state that abortions are caused by pelvic kidneys which are often mistaken for ovarian cysts, and they point also to the danger to mother and baby in full-term pregnancies.

Frank³ reported a patient (Case 3), aged thirty-five years, who had 2 deliveries and 19 spontaneous abortions, presenting a globular mass deep in the left posterior pelvis which felt to him like the lower pole of a kidney. Diagnosis was confirmed by pyelography and proved by operation which was done for other reasons. The kidney was found to be cystic but was not removed. Any lesion which may occur in the normally placed kidney may be found in the ectopic pelvic kidney. An example of such a puzzling urinary tract condition is the following:

CASE 1.—H. H. (No. 300215.) (Courtesy Dr. T. N. Hepburn.) Female, aged twenty-nine years, complaining of incontinence of urine since operation at age of six, at which a supposed abscess of the left ovary was drained both abdominally and vaginally. A urinary fistula into the vagina resulted which resisted several attempts at closure. This patient proved to have a third rudimentary kidney located as usual above the normal kidney on the left and emptying into the vestibule, as indicated by vestigial remains of its ureter. The original operation was, in fact, a drainage of an infected hydroureter, and the patient was ultimately cured by an extensive resection of the anomalous third urinary tract.

Ectopic pelvic kidneys have been very rarely observed in the Hartford Hospital in female patients. One personal instance is as follows:

CASE 2.—H. H. (No. 311669.) Patient, aged twenty-eight years, came to operation for endometriosis of the ovaries. Before operation, an ectopic kidney on the left was thought to be a retroperitoneal fibroma. Pyelographic study confirmed

by operation showed this to be an ectopic left kidney just above the pelvic brim, rotated 180 degrees on its vertical axis, so that its pelvis lay to the left and the cortex to the right. The kidney functioned normally and was not disturbed.

2. TUMORS OF BONE AND CARTILAGE ARISING FROM THE LUMBOSACRAL VERTEBRAS AND PELVIC BONES

Osteochondromas and similar tumors, both benign and malignant, are usually so hard to palpation that x-ray study is obviously called for and leads to diagnosis and treatment in conjunction with an orthopedic surgeon. According to Ewing,⁴ the most common tumors in this region are giant cell tumors, multiple myelomas, and osteogenic periosteal sarcomas.

3. INFECTIONS OF THE RETROPERITONEAL SPACE

CASE 3.—H. H. (No. 198290.) (Courtesy Dr. A. M. Rowley.) Female, aged twenty-nine years. When asked to see this patient twelve hours before her death and while she was under an anesthetic, I found a large boggy mass in the pelvis behind the rectum, displacing it to the right. Under guidance of fingers in the vagina and rectum, I punctured the mass through the left vaginal fornix, evacuating a large amount of thick yellow odorless pus which showed *Staphylococcus aureus* on culture. The history of this patient showed an increasing fever for fourteen days with inability to walk. On the second day of her illness her physician treated her for pelvic inflammatory disease. Seven days before death she showed motor and slight sensory disturbances of the lower extremities, high white blood count and high cell count in the spinal fluid, increasing incontinence of urine, a positive blood culture of *Staphylococcus aureus*, and a urine which contained *B. coli* and a non-hemolytic streptococci. X-rays showed no evidence of osteomyelitis. Autopsy revealed a *Staphylococcus aureus* abscess 15 by 10 by 10 cm. in the hollow of the sacrum behind the rectum, which had dissected the large nerve trunks of the sacral plexus. It could be traced to within 2 cm. of a healed furuncle on the left buttock about 5 cm. behind and to the side of the anus. Autopsy revealed also an operative puncture wound in the deep culdesac of Douglas from which a general peritonitis could have developed. Though the outcome in this case was not altered, it clearly indicates the ideal approach to such masses is posteriorly to one side of the tip of the sacrum or even directly through the rectum.

CASE 4.—H. H. (No. A 739.) Osteomyelitis of the fifth lumbar vertebral body. (Courtesy Dr. O. R. Witter.) I was asked to make a pelvic examination on an unmarried woman, twenty-four years of age, four days after onset of acute left lumbar pain with fever. The pelvic organs were normal. There was a great tenderness at the lower end of the left sacroiliac joint by rectal touch, and I suggested suppuration of this joint cavity as a possibility. Three days later at autopsy, a retroperitoneal bulging mass was found over the left posterior pelvic wall covering the sacroiliac synchondrosis. Ten cubic centimeters of thick green *Staphylococcus aureus* pus was obtained, originating from many areas of osteomyelitis in the body of the fifth lumbar vertebrae. The pus had burrowed through the obturator foramen toward the head of the femur and beneath the gluteus muscles. Generalized sepsis was present with abscesses in the lungs and kidneys.

4. EARLY PSOAS ABSCESS

No case of early psoas abscess was encountered by the Gynecological Service in the Hartford Hospital in recent years, and it is not likely that serious errors would arise, for if the abdomen were entered for correction of other serious pelvic conditions, as in the case reported by Frank,³ the location of the mass behind

the iliac vessels would indicate the nature of the lesion. As in Frank's case, such masses must not be aspirated and the patient should be placed under appropriate orthopedic care. It is to be hoped that the possibility of psoas abscesses will not be beyond the mental horizon of the gynecologist who may happen on such a rare case in these days of narrowed specialism and diminished incidence of tuberculosis.

In one case on the general Surgical Service at the Hartford Hospital, an unrecognized psoas abscess was inadvertently drained at laparotomy. The patient survived but a sinus tract has persisted.

5. CHRONIC ILIAC ADENITIS

Frank³ also reported a case of massive adenitis of the iliac glands secondary to an inflammatory focus of the lower extremity. Differential diagnosis in this case included malignant thrombosis of the external iliac veins, osteosarcoma of the left pubic bone and carcinoma of the ovary. Exploratory operation disclosed a large conglomeration of swollen lymphatic glands along the course of the external iliac vessels. An inguinal gland on biopsy showed nonspecific inflammatory hyperplasia with reticular cell proliferation.

6. EMBRYOLOGIC CYSTIC REMAINS OF THE WOLFFIAN BODY

CASE 5.—H. H. (No. 284439.) (Courtesy Dr. E. R. Lampson.) Female, aged forty-one years, para ix. Had been well since cholecystectomy three years previously. She suffered from needle-like pains in the right flank for four to five months, increasing in severity. A mass the size of a hen's egg high in the right groin was at first taken to be a hydroureter, but x-ray study showed it to be independent of the urinary tract and lateral to the cecum. This proved to be a cyst 7 cm. in diameter, lined by a single layer of flattened cuboidal epithelium, and was easily removed.

7. RECURRING RETROPERITONEAL FIBROMYOMAS

CASE 6.—H. H. (No. 312699.) (Courtesy Dr. A. M. Rowley.) Female, single, aged fifty-two. At age forty-three, the uterus had been removed above the cervix for fibromyomas which were shown to be of the usual variety. On her second admission eight years later, a tumor 16 by 3 by 9 cm. was removed from the upper abdominal retroperitoneal tissue behind the small bowel and its mesentery. At her third admission four months later, several more tumors were removed from the same location, the largest of which was 12 cm. in diameter. At her fourth admission four months later, she complained of low back pain extending down her right thigh and a bearing-down sensation in the lower abdomen. Several large tumors were removed from the retroperitoneal tissues behind the small bowel, the largest of which was 20 cm. in diameter, and one of the smaller tumors was removed with great difficulty from its location adjacent to the aorta. Careful review of all the slides failed to show any nerve tissue or evidence of malignancy. Careful search of all the retroperitoneal tissue was made at the last operation and no further nodules were found.

Within four months after the patient's previous operation, she again presented herself with a rapidly growing tumor of the same general description and location. In addition, this time she had a tumor 4 or 5 cm. in diameter in the upper end of the biceps muscle which had grown within the last three to four months. Further operative treatment is contemplated and will be reported later.*

*Six months after previous operation, numerous similar fibroids were removed at laparotomy from the retroperitoneal tissues to the right and behind the ascending colon. The cellular structure showed no anaplasia and Masson's stain shows no nerve elements. The mass in the biceps muscle disappeared spontaneously.

8. RETROPERITONEAL LIPOMAS

Numerous reviews of these interesting tumors emphasize not only the tendency to sarcomatous degeneration but also the great danger of very large tumors due to injuries of the blood vessels and of the bowel. Mechanical difficulties at times may be insurmountable even for the most skillful surgeon. These tumors are often mistaken for large ovarian cysts.

CASE 7.—H. H. (No. 179996.) (Courtesy Dr. C. H. Elliott.) The patient aged forty-two years, nullipara. This patient was admitted with the diagnosis of cystadenoma of the ovary, probably malignant. She had been operated upon for fistula in ano elsewhere four years previously, but as she weighed nearly 260 pounds at that time, her surgeon can be excused for making no note of an abdominal tumor. During the past three years she has lost 70 pounds and only recently noticed an abdominal mass. The menses were normal. The upper abdomen appeared to be filled by a solid tumor which, however, gave a highly suggestive fluid wave. The diaphragm was pushed high and the uterus was pushed forward by a semisolid feeling mass in the pelvis which seemed to be continuous with the upper abdominal tumor. X-ray examination showed the viscera displaced to the left. At operation numerous retroperitoneal lipomas were encountered, all of which could not be removed. Four separate masses totaling 6,000 gm. were removed, but several masses in front of the left kidney and below the pelvic brim had to be left. A fecal fistula developed, and in a desperate attempt to close the fistula three months later, because of progressive weakness and vomiting, the patient died. Autopsy revealed a putrid peritonitis which involved both the peritoneal cavity and the remaining lipomas and retroperitoneal tissues. The tumors which remained weighed 5,800 gm.

Retroperitoneal lipomas usually extend within the confines of the abdominal cavity, but the case reported by Deupert⁵ indicates that these tumors may seek room for extension outside the pelvic cavity by way of the pelvic foramina. He found a huge lipoma with sarcomatous degeneration emerging through the obturator foramen from within the pelvis. He removed the intrapelvic portion by morcellation through the obturator foramen under guidance of laparotomy. The patient survived the immediate operation but shortly developed a recurrence.

9. RETROPERITONEAL NEUROLIPOMA

In spite of the general opinion that such cases as the two previous ones owe their origin in part to nerve tissue, no histologic proof of this could be shown. The following case, however, was such an example. (Personal case—patient operated upon at St. Francis Hospital.)

CASE 8.—Patient, aged thirty-four years, whose chief complaint was sterility of five years' duration. Shortly after her marriage, a fibroid tumor was diagnosed and observed for two years without growth. I found an anteфлекed, small fibroid uterus, and in addition a firm tumor mass filling the entire hollow of the sacrum and extending well above the pelvic brim in front of the promontory. X-ray showed no evidence of osteochondroma. At operation three small fibroids were enucleated from the fundus and a retroperitoneal tumor was found covering almost the entire surface of the sacrum, extending 3 to 4 cm. above its pelvic brim. The right ureter coursed over its right edge for a distance of 10 cm. The tumor was removed through a long midline peritoneal incision mostly by sharp dissection, for numerous sympathetic nerve fibers bound down the mass in a manner which reminded one of the restraint under which Gulliver was placed by the Lilliputians. The internal iliac vessels on both sides were laid bare with difficulty, and one branch of a large vein deep in the pelvis was injured, causing considerable bleeding. This was

ligated, a transfusion was given, and uneventful recovery ensued. Pathologic examination showed a neurolipoma about the size and shape of a plump full-term placenta.

10. BENIGN TUMORS OF THE PERIPHERAL AND AUTONOMIC NERVOUS SYSTEM

Whether the previous case arose from, or was complicated by, nerve tissue, numerous examples are found of true nerve tissue tumors such as the following:

CASE 9.—H. H. (No. 294395), single, aged forty, suffering from gradually advancing multiple sclerosis of five years' duration. The presenting symptoms were urinary urgency and frequency of voiding. Examination showed a cystic feeling tumor occupying the left half of the pelvis and displacing the normal uterus to the right. Operation was done under a diagnosis of ovarian cyst and disclosed a bright red, cellular tumor, 12 by 9 by 9 cm., lying retroperitoneally two-thirds below and one-third above the pelvic inlet and to the left and behind the sigmoid. Removal was accomplished without great difficulty by sharp dissection of the many thread-like nerve filaments which bound the tumor to the lateral pelvic and sacral walls. The blood supply of the bowel was not injured, and the patient has remained well for two years. Microscopic examination showed a very cellular neurofibroma with fasciuli of cylindrical and fusiform cells which are uniform in size and stain and which show no anaplasia and only a few regularly formed mitoses. A few areas of myxomatous degeneration were noted.

CASE 10.—Tumors of the nerve sheath, so well summarized by A. P. Stout,⁶ have not been demonstrated beyond question in our experience. The following case, however, is very suggestive and presented a picture similar to that reported by R. T. Frank⁷ under the name of schwannoma.

H. H. (284966), aged thirty-seven years, para i. The presenting symptom was pain in the right sacroiliac region, radiating down the right leg and into the perineum which had been developing since a very difficult high forceps delivery eleven years previously, followed by a febrile puerperium. She stated that her anesthesia had been incomplete and she remembered the pain down the leg at the time of the forceps delivery. Extensive urologic, orthopedic, and neurologic advice had been sought under excellent circumstances. Prominent gynecologists had advised removal of the tube and ovary on this side. I could find no abnormality of the adnexa, but movement of the cervix forward and away from the right side caused pain. Just above the right ischial spine in the region of the sacral plexus, there was a distinct cystic feeling mass 1 by 2 by 4 cm., pressure on which made the patient cry out with pain identical with her chief complaint. There were no neurologic symptoms in the distribution of the right sacral plexus and proof of the nature of this tumor could not be obtained since she refused operation. I believe, however, that this may well have been neurilemoma or schwannoma of traumatic origin.

11. RETROPERITONEAL MYOSARCOMA

CASE 11.—H. H. (No. 310917.) (Courtesy Dr. G. H. Howe.) Patient aged fifty-eight years, para ii. Patient entered with a history of enlarging abdominal mass during the past three to four months, nausea and vomiting, loss of weight and strength, and sharp attacks of pain in the left upper quadrant and epigastrium. Twenty years previously one ovary and part of the other were removed together with the appendix. Her abdomen was enlarged to the size of an eight months' pregnancy by a firm mass which was dull to percussion. Under diagnosis of carcinoma of the ovary the abdomen was opened, disclosing a large amount of amber colored fluid and papillary implantations throughout the peritoneum with metastatic involvement of the omentum and intestines. A cystic mass the size of a large orange

arose from the region of the right ovary. A large specimen of omental tissue was removed, and the patient died on the sixth day from a secondary hemorrhage. The essential findings at autopsy were a tumor mass lying lateral to the ascending colon retroperitoneally, associated with a cyst about 10 cm. in diameter which had a thick fibrous wall. There was no connection with the genital organs. Metastases were found in the adrenal, the seventh rib and throughout the peritoneum.

Microscopic study showed a highly malignant tumor of large multinucleated cells with slightly eosinophilic cytoplasm. The cells were fusiform in shape with many fibrillary extensions. Some cells were small and round. The cecum was infiltrated by the tumor only as far as the mucous membrane. In view of the multinucleated and irregular mitoses, the fascicular arrangement and fibrillary structure, our pathologists leaned toward diagnosis of a malignant neurogenic tumor, possibly a glioma, but further study, in which Dr. James Ewing concurs, led to a diagnosis of myosarcoma.

12. RETROPERITONEAL SARCOMA

Many reviews in the literature point to the relative frequency of sarcoma of the retroperitoneal connective tissues, either as primary growths or as sarcomatous degeneration of tumors which are otherwise benign.

CASE 12.—H. H. (No. 287880), aged thirty-four years, gravida iii, para ii. Her last pregnancy was an abortion one year previously. On admission this patient was again in the third month of pregnancy. Her uterus was pushed high to the left by a retroperitoneal mass projecting into the right pelvis and reaching as high as the right iliac fossa behind the cecum. This tumor was hard and smooth, the size and shape of a flattened grapefruit. Another small tumor was noted at its upper pole. At operation the ureter was plainly visible in front of the mass. The uterus was emptied by hysterotomy with ligation of the tubes. A biopsy was taken which showed distinctly anaplastic groups of round cells with an indefinite intercellular supporting stroma. The nuclei were round and deeply staining with a diffuse chromatin structure. Diagnosis was made of retroperitoneal sarcoma of mesoblastic origin. Subsequently this patient received intensive deep x-ray therapy which apparently retarded the growth until her death occurred four and a half years after operation. The nerve supply of the right leg was seriously involved even from the first.

CASE 13.—H. H. (No. 258070), aged sixty-five years, single. On her first admission, radium and x-ray therapy were given for papillary adenocarcinoma of the fundus (Grade 3, Healy). Five weeks later panhysterectomy was done and no extension of the growth was observed. Four months later a thickening of the left parametrial tissue was observed, and on x-ray study a retrorectal mass 10 cm. in diameter was diagnosed as a recurrence of the uterine carcinoma and further x-ray radiation was given over the pelvic region. No improvement occurred and a biopsy of the growth was obtained at exploratory laparotomy from a soft retroperitoneal mass behind and to the left of the sigmoid and rectum. Microscopic study showed a very cellular malignant tissue, consisting of moderately large cells containing large, oval or round vesicular nuclei which occupied almost the entire cell. Some cells tended to be spindle-shaped. Mitoses were prominent though for the most part regular in form. Diagnosis was made of sarcoma of mesoblastic origin. This patient died a few weeks later and at autopsy diagnosis of spindle-celled sarcoma of the retroperitoneal space was substantiated. In addition, numerous metastatic nodules were found in the liver and lungs which showed an adenomatous structure consistent with metastases of the original adenocarcinoma of the fundus.

13. LYMPHOBLASTOMA

CASE 14.—H. H. (No. 317246.) (Courtesy Dr. C. T. Bingham.) Patient aged forty-nine years, para iii. Biopsy showed a typical lymphoblastoma. This patient died about two months after exploratory operation and at autopsy diagnosis was confirmed. Death occurred from uremia caused by blockage of both ureters by the tumor. Deep x-ray therapy was only of temporary value. It was notable in this patient that there was no general glandular or splenic enlargement.

14. CHORDOMA

The recent review of chordomas by R. E. Babreys calls attention to this fatal type of tumor originating from fetal notochord. Those of interest to the gynecologist are particularly the antesaeral variety, of which 41 were reported out of 150 in the literature. These tumors have a tendency to surround the rectum, the infiltration and fixation being even more extensive than in carcinoma of the rectum.

CASE 15.—H. H. (No. 314266.) (Courtesy Dr. W. Standish.) Patient, aged three years, presented a mass in the left inguinal region, and one the size of a golf ball just in front of the coccyx and behind the rectum, of about three to six weeks' duration. Biopsy obtained under anesthesia, at which time careful rectal examination was done which showed a friable gray cellular tissue having no definite capsule, and in some areas being slightly opalescent. This was made up of neoplastic cells, lining and almost filling irregular spaces, sometimes in papillary formation. The cells were irregular in shape with a very sharp cell margin and a clear vacuolated cytoplasm containing large, oval or round nuclei with rather delicate chromatin network. The nucleoli were poorly seen, small, and frequently multiple. There were many mitoses and considerable anaplasia. Diagnosis was made of a malignant tumor, probably an embryonal carcinoma, possibly a chordoma. This patient died shortly after leaving the hospital with metastases in the spine and lungs. Deep x-ray radiation had little effect.

15. RETROPERITONEAL DERMoids OR TERATOMAS

No instances were noted of retroperitoneal dermoids or teratomas. Ewing⁴ classifies three types: (1) tridermal teratomas, (2) epidermoid rests of wolffian duct, and (3) true dermoids. He states that dermoid cysts of the pelvic connective tissue are rare.

At the onset of this study, it was hoped to present a classification of retroperitoneal masses which the gynecologist might expect to encounter. It soon became evident, however, that a complete catalogue of all the tumors which have been recorded as arising in this region would resemble a treatise on general pathology. As far as neoplasms are concerned, classification of neoplastic diseases offered by Ewing for the whole body would serve equally as well for the retroperitoneal region. Suffice it to say that the operator must bear in mind the various possibilities, rare though they may be.

SUMMARY

Attention has been called to the great variety of neoplasms and other masses which may be encountered in the retroperitoneal tissues in and about the pelvis. Brief case histories of instances coming under observation have been given.

For the gynecologist to treat successfully the wide variety of lesions which may be encountered, it is necessary for him to know well the anatomy of this region, especially its blood and nerve supply, and also to understand various pathologic processes which may surprise him.

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DISCUSSION

DR. I. C. RUBIN, NEW YORK, N. Y.—Among 5,600 cases admitted to the Gynecological Service of the Mount Sinai Hospital for a period of eight years there were 4 that could come under this grouping of retroperitoneal pelvic tumors. Two were referred to by Miller, and reported by Frank, a lymphangioma and a schwannoma. The incidence was about one in 1,400 cases.

Iliac lymphadenitis is not, properly speaking, a retroperitoneal tumor. This type of pelvic mass occurs perhaps a little more frequently than is commonly appreciated. Nor are sacral kidneys retroperitoneal tumors, in the strict pathologic sense.

There is apparently a reason for the infrequency of pelvically placed retroperitoneal tumors. Retroperitoneal tumors, especially the solid variety, arise as a rule from the three organs, namely, the pancreas, the kidneys, and the suprarenals. In the female pelvis such tumors may also originate from the Wolffian and Gärtner's ducts, or from components of the ovary.

One of the retroperitoneal cysts that we encountered was a tumor occupying the entire abdomen and presenting a picture of a woman at term pregnancy. It was possible to feel the lower pole of the tumor by bimanual examination. There was a fluid wave in both flanks. An intravenous urograph failed to give us any aid because of lack of concentration of the dye. By transuterine pneumoperitoneum, a huge mass was demonstrated in the abdomen which was neither connected with the liver nor the spleen, nor with the depth of the pelvis. Its fixation moreover gave us the impression that we were dealing with a retroperitoneal cyst. At laparotomy the tumor was found to arise from behind the posterior parietal peritoneum, to the right of the ascending colon. It was shelled out readily as far as the junction of the ureter to the pelvis of the right kidney which was found to be hydronephrotic. We thought it might therefore be a cyst of the kidney, but when removed it was shown to be a simple cyst with an endothelial lining, some smooth muscle strands and connective tissue, in other words, a large retroperitoneal cyst which had nothing to do with the kidney itself.

There is one kind of cyst that has not been emphasized by Dr. Miller and which is more commonly encountered by gynecologists. In this type the lower pole reaches almost to the level of the perineum, and we all know how difficult it is to shell it out from its deepest portion. Occasionally it is necessary to marsupialize it in order not to make the operation too extensive.

The tumors that I have just referred to as being supposedly of inflammatory nature, the tumors that give rise to pelvic tenesmus, and which lead you down into the obturator fascia, are properly classified, I think, as retroperitoneal tumors be-

cause they most likely arise from the rests of the Wolffian and Gärtner's ducts, which are commonly met with in that area. They are ordinarily regarded as intraligamentous cysts but may properly be called retroperitoneal cysts.

DR. ALEXANDER M. CAMPBELL, GRAND RAPIDS, MICH.—I wish to report an unusual case of a woman who was referred to us recently with the diagnosis, by her family physician, of ovarian cyst. The abdomen was almost the size that one would find in a full-term pregnancy. The only disturbance from which she suffered was shortness of breath.

A pelvic examination revealed a normal uterus and normal ovaries. On an exploratory operation we discovered an enormous retroperitoneal cyst which was approached by opening the gastrocolic omentum and stitching the posterior peritoneum to the parietal peritoneum and leaving a large circular opening exposed for a week. This opening was packed with gauze and on the eighth day the cyst was evacuated and five quarts of a chocolate fluid were taken from this cyst. The fluid had digestive qualities. A portion of the capsule of the tumor was removed for pathologic examination and the cyst showed no epithelial lining. It was undoubtedly an inflammatory cyst of the pancreas. The cyst cavity was packed with iodoform gauze and it is gradually closing.

RADIUM IRRADIATION FOR BENIGN HEMORRHAGE

WITH A TWO TO TWENTY-YEAR REVIEW OF 1437 CASES

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RADIUM irradiation is now generally accepted as the method of choice in the treatment of certain types of uterine hemorrhage of benign origin. The chief disadvantage of the treatment is that its success is dependent largely, if not entirely, upon the inhibiting or destructive action of the irradiation upon the ovarian endocrine system. This destructive action is one that should definitely be considered in evaluating this method of treatment. Many surgeons are prone to base the success or failure of the treatment solely by the effect it has on the hemorrhage.

The following report is the result of a study made of all patients with benign uterine hemorrhage treated with intrauterine radium irradiation in the Gynecologic Division of the Hospital of the University of Pennsylvania from 1916 to 1935 inclusive. In addition to the reports of the routine follow-up, and with a view to bringing the records up to date and determining, as far as possible, the ultimate outcome of each case, a questionnaire was sent to each patient. Those cases residing in or near Philadelphia were requested to return for examination and personal interviews. In all, 1,437 patients treated by radium irradiation for benign hemorrhage were studied; including 750 cases of functional

hemorrhage and 687 cases of myomas. Of these, 1,006 patients have been followed for two years or more (521 functional hemorrhage and 485 myoma uteri). Records of 184 of the myoma cases and of 116 cases of functional hemorrhage are available for follow-up study, for periods covering from ten to twenty years. Many patients were examined and questioned personally. As regards the development of menopausal symptoms induced by the irradiation, the patient's own statement has been the criterion upon which the statistical study is established. The fact that our personal opinion, based upon answers received at interview with patients, does not always accord with the patient's view, has not been considered in deciding this point. Thus some patients stated that the menopausal symptoms were severe, whereas questioning brought out the fact that they were probably mild and caused but little discomfort; in other instances, it appeared that the menopause developed in a normal manner. It is obvious, therefore, that it is difficult to determine this accurately since the pain and discomfort thresholds vary so markedly in different patients. In passing, it may be stated that the group interviewed personally yielded decidedly better results in this respect than did the answers secured from the questionnaires.

Although the severity and duration of the menopausal symptoms that may develop after irradiation are of importance in evaluating the results of the treatment, this is, as previously stated, a difficult point to determine with accuracy, particularly when dealing with answers to questionnaires. For this reason, this feature is not stressed in the following report; it has been dealt with in detail in the study by Keene and Payne* published in 1933. No result has, however, been classed as satisfactory in which the patient stated that the menopause was so severe that it incapacitated her or in which the pathologic bleeding was not relieved permanently.

The results secured in the myoma and in the functional hemorrhage cases have been separated. A special effort has been made to analyze such late results and complications as might develop ten or more years after irradiation, as well as the effect of the treatment upon fertility and subsequent pregnancy.

As a routine measure a preliminary diagnostic curettage was performed in each case. No case of carcinoma has ever been overlooked, with possibly one exception. This was a case in which a histologic diagnosis of hyperplasia was made; seven and one-half months later a second curettage was performed and carcinoma was diagnosed. Hysterectomy was performed and a carcinoma measuring 1 by 0.5 by 0.5 cm. was found in one cornu.

Indications.—In the John Goodrich Clark Clinic the indications for radium irradiation in the class of cases under discussion have changed but little since 1916, although dosage and filtrations have undergone

*Keene, Floyd E., and Payne, Franklin L.: Surg. Gynec. Obst. 56: 322, 1933.

modifications. Our indications for radium therapy for benign hemorrhage are: patients suffering from pathologic bleeding in whom more conservative measures have failed, who are at or near the menopause and in whom other pelvic complications are absent; in the myoma group, patients having tumors not larger than a four months' pregnancy. Numerous patients not entirely ideal have also been treated by irradiation, the associated conditions being such as to make hysterectomy unduly hazardous or undesirable.

Contraindications.—The contraindications to irradiation are:

1. When doubt exists as to the accuracy of the diagnosis.
2. The presence of intraperitoneal lesions other than those responsible for the bleeding and which require surgical intervention.
3. Rapid growth in the case of a supposed uterine myoma.
4. Associated fundal carcinoma.
5. Pressure symptoms.
6. Softening or other evidence of degeneration.
7. Inflammatory lesions within the pelvis, especially those of the adnexa.
8. The presence of neoplasms larger than a four months' pregnancy.
9. Submucous tumors, especially, if they are pedunculated.
10. Myomas in young women.
11. Anemia markedly out of proportion to the bleeding.
12. Obstructing tumors or malformations that prevent the proper application of the radium.
13. Radiophobia.
14. The presence of cervical myomas.
15. Pregnancy.
16. Highly nervous women.
17. Previous pelvic operations.
18. Painful myomas.
19. Myomas after the menopause.

These indications and contraindications are not governed by a hard-and-fast rule; for example, an associated cardiac lesion may make irradiation of a myoma advisable which otherwise would be treated by hysterectomy or myomectomy; or in an associated fundal carcinoma irradiation may be the method of choice because of extreme obesity or for other special reasons.

In the analysis of the group of cases discussed in this paper it should be remembered that there are included a large number of the patients suffering from severe anemia, due either to functional hemorrhages or to myomas, who have entered our clinic during the last twenty years. Although we are aware that this type of case is not ideal for irradiation, we have often been forced to resort to this method of treatment when more conservative measures failed. In recent years, most of our patients who were markedly anemic have received preliminary blood transfusions. Furthermore, the John Goodrich Clark Clinic was one of the pioneers in the use of radium in America, and therefore dosage and technique were not so well established in the earlier cases as they are at

the present time. Many of these patients were treated before the subject of endocrinology had been developed and could neither be studied nor treated for hormonal imbalance. Nevertheless, the series under discussion embraces all patients treated during this more or less experimental period.

A large proportion of our patients with functional bleeding had been treated by medical measures without result. In the more recent groups medical measures had been supplemented by endocrine therapy in a number of cases. Curettage had been previously performed elsewhere in a proportion of cases and in these irradiation was resorted to only after failure of the more conservative measures.

From 1916 to 1931, the radium filtration was 1 mm. of brass or 0.5 mm. of platinum; from 1931 to 1935, 1 mm. of platinum was employed. An additional filter of 2 mm. of red rubber tubing has been used routinely.

Optimum Dosage.—If a dosage large enough to destroy the ovarian function is administered, complete cessation of bleeding can be secured in practically all cases. As a result of such treatment, however, the irradiation menopause is established. The severity and character of the symptoms are the same as those of the menopause which follows a bilateral oophorectomy. Loss of ovarian function causes varying degrees of discomfort and is dependent upon many factors, the nervous stability of the patient, her age, temperament, and many other conditions.

The menopause was one of the chief subjects discussed before the Eighth Congress of the Association of Gynecologists and Obstetricians of the French Language. At this meeting, Barrett and other members of a committee reported that, among 1,000 women studied, 89.7 per cent were able to carry on their usual occupations without interruption during the menopause, and that 15.8 per cent were entirely free from unpleasant symptoms during this period.

The great majority of patients suffering from benign hemorrhage are under forty-five years of age, and a considerable proportion are much younger. In other words, a relatively large number of these patients may be expected to undergo discomfort as a result of a castrating dose of radium, and a definite percentage will suffer acutely for years. Furthermore, some of these patients are in the childbearing age, and the sterilization that results from irradiation is a factor to be taken into serious consideration. This applies especially to those patients suffering from functional hemorrhage, who, considered as a group, are younger than those who suffer from myomas.

In contrast to the disadvantages just described must be mentioned the efficacy of the treatment in arresting hemorrhage, its low attendant mortality and morbidity, and the shortness of the period of convalescence. The fact that surgery is by no means always the ideal method of treatment should also be taken into consideration. The point which

we wish to stress is that radium is a highly potent and, so far as ovarian function is concerned, a destructive agent. In spite of this unfavorable action, irradiation is the most satisfactory method of treatment at our command at present in certain cases.

An important point to be borne in mind is that the selection of cases for irradiation and the dosage should be carefully considered. Irrevocable damage may be done by ill-advised irradiation. The efficacy of the remedy in stopping hemorrhage and the ease with which it may be applied constitute definite hazards in this form of treatment, particularly in patients in the childbearing period. As a result of these observations, efforts have been made to modify the dosage of radium so that hemorrhage will be checked but without completely sacrificing the ovarian function. Of course, it is obvious that a dosage of this size is less certain and less permanent in its results, but is, we believe, the method of choice. To determine the ideal dosage is by no means easy, and it is only by a careful and unbiased analysis of the end-results in groups of cases during the various decades that even an approximately safe and effective dosage can be arrived at. It is our belief that in the past, particularly in the earlier cases, too heavy irradiation has been employed. This applies especially to the younger group of patients.

Table I shows the percentage of menopausal symptoms that developed in 496 of the patients irradiated for *functional hemorrhage*, arranged according to age.

TABLE I. PERCENTAGE OF PATIENTS EXHIBITING MENOPAUSAL SYMPTOMS AFTER IRRADIATION FOR FUNCTIONAL HEMORRHAGE (496 CASES)*

AGE IN YEARS	PATIENTS IRRADIATED NUMBER	MENOPAUSAL SYMPTOMS PER CENT
Less than 20	15	33
20 to 30	74	24
30 to 40	137	67
40 to 50	229	68
Over 50	41	70

*Note low incidence of menopausal symptoms in patients less than thirty years of age. Definite information regarding menopausal symptoms was not available in 25 additional cases followed up.

Table II shows the percentage of menopausal symptoms that developed in relation to age in 471 of the patients irradiated for *uterine myomas*.

TABLE II. PERCENTAGE OF PATIENTS EXHIBITING MENOPAUSAL SYMPTOMS AFTER IRRADIATION FOR MYOMAS (471 CASES)*

AGE IN YEARS	PATIENTS IRRADIATED NUMBER	MENOPAUSAL SYMPTOMS PER CENT
Less than 30	9	33
30 to 40	76	81
40 to 50	288	57
Over 50	98	55

*Definite information regarding menopausal symptoms was not available in 14 additional cases followed up.

Tables I, II, and III, indicate that among the patients under thirty years of age, menopausal symptoms following irradiation were present in about 30 per cent of cases. The relative infrequency of the menopausal symptoms in these groups as compared with those made up of

TABLE III. PERCENTAGE OF PATIENTS EXHIBITING MENOPAUSAL SYMPTOMS AFTER IRRADIATION FOR FUNCTIONAL HEMORRHAGE AND MYOMA UTERI

AGE IN YEARS	PATIENTS IRRADIATED NUMBER	MENOPAUSAL SYMPTOMS PER CENT
Less than 20	15	33
20 to 30	83	29
30 to 40	213	71
40 to 50	517	62
Over 50	139	56
Total	967	59

older patients may perhaps be explained by the fact that the average dosage was considerably smaller among the former and that the ovaries of young women are probably more resistant to the destructive action of the rays than are those of the older patients, or they may recover more easily from the effects of treatment.

Table IV shows the total number of patients who have become pregnant following irradiation, the total number of pregnancies, and the condition of the fetuses at the termination of pregnancy. The infrequency with which pregnancy occurred, and the high percentage of nonviable fetuses in this series are worthy of note.

TABLE IV. POSTIRRADIATION PREGNANCIES IN ENTIRE SERIES

DIAGNOSIS	PATIENTS IRRADIATED	PATIENTS PREGNANT	TOTAL PREGNANCIES	LIVING CHILDREN	NONVIALE FETUSES	UNDELIVERED PREGNANCIES
Functional hemorrhage	521	18*	28	12	13	3
Myoma uteri	485	2	3	3	0	0
Total	1006	20	31	15	13	3

*Two patients with questionable early pregnancies at last follow-up not included.

Table V is a detailed summary of the patients who have become pregnant following irradiation, as well as the number of stillbirths, miscarriages, and abortions.

In our series of cases, pregnancy following irradiation has been of infrequent occurrence, probably because relatively few of the patients who were subjected to this form of treatment were in the childbearing age. Furthermore, myomas were present in nearly half of the patients, and since these neoplasms tend in themselves to produce sterility, this is also a factor in preventing conception, as well as in producing abortion if conception should take place. In the cases of functional hemorrhage, endocrine imbalance may explain the high proportions of sterile patients and the frequency of nonviable fetuses.

As a result of his extensive clinical and experimental studies, Douglas P. Murphy reached the conclusion that preconception irradiation had little if any effect upon subsequent pregnancies, except to cause sterility. The number of patients in our series in whom pregnancy followed irradiation is a small one, far too small to permit conclusions to be drawn regarding the fate of the embryo.

TABLE V

<i>A. Summary of Pregnancies Following Irradiation for Functional Hemorrhage</i>	
4 patients	Each, 1 full-term pregnancy
1 patient	2 full-term pregnancies
1 patient	1 full-term pregnancy; 1 premature delivery, the infant living two days
1 patient	1 full-term pregnancy (toxemia); 1 full-term pregnancy; 1 miscarriage
1 patient	1 full-term pregnancy; 2 stillbirths
1 patient	1 stillbirth
1 patient	2 stillbirths
1 patient	7 months' premature infant
1 patient	1 miscarriage; again pregnant at time of last follow-up
1 patient	3 miscarriages
2 patients	Each, 1 miscarriage
1 patient	1 induced abortion for therapeutic reasons
2 patients	Each pregnant last follow-up
1 patient	1 possible miscarriage
1 patient	1 questionable pregnancy last follow-up
<i>B. Summary of Pregnancies Following Irradiation for Myomas</i>	
1 patient	1 premature pregnancy, the infant living
1 patient	2 full-term pregnancies

Table VI shows the proportion of menopausal symptoms following irradiation and the satisfactory results secured in the functional hemorrhage cases.

TABLE VI. PROPORTION OF MENOPAUSAL SYMPTOMS AND SATISFACTORY RESULTS FOLLOWING IRRADIATION IN VARIOUS DOSAGES FOR FUNCTIONAL HEMORRHAGE

RADIUM DOSAGE MG. HR.	NUMBER OF PATIENTS	MENOPAUSAL SYMPTOMS PER CENT	NUMBER OF PATIENTS	SATISFACTORY RESULTS PER CENT
500 or less	219	42	231	75
600-1000	118	70	120	83
1200-1500	135	80	141	92
1500 and over	24	79	29	83
Total	496*	61	521	82

*Definite information regarding menopausal symptoms could not be obtained in every case followed up, but was available in the vast majority.

TABLE VII. PROPORTION OF MENOPAUSAL SYMPTOMS AND SATISFACTORY RESULTS FOLLOWING IRRADIATION IN VARIOUS DOSAGES FOR MYOMA UTERI

RADIUM DOSAGE MG. HR.	NUMBER OF PATIENTS	MENOPAUSAL SYMPTOMS PER CENT	NUMBER OF PATIENTS	SATISFACTORY RESULTS PER CENT
500 or less	35	58	42	67
600-1000	123	55	125	86
1200-1500	271	59	275	84
1500 and over	42	57	43	81
Total	471*	56	485	85

*Definite information regarding menopausal symptoms could not be obtained in every case followed up.

In connection with Table VIII, it will be noted that the menopausal symptoms are materially less in patients who received a dosage of less than 600 mg. hours, but the satisfactory results secured are correspondingly diminished with the smaller dosage. The effect of irradiation in dosages over 600 mg. hours was practically constant both in regard to the percentage of menopausal symptoms produced and the satisfactory results achieved.

TABLE VIII. PROPORTION OF MENOPAUSAL SYMPTOMS AND SATISFACTORY RESULTS FOLLOWING IRRADIATION IN VARIOUS DOSAGES FOR ENTIRE FOLLOWED-UP SERIES

RADIUM DOSAGE MG. HR.	NUMBER OF PATIENTS	MENOPAUSAL SYMPTOMS PER CENT	NUMBER OF PATIENTS	SATISFACTORY RESULTS PER CENT
500 or less	254	44	273	74
600-1000	241	62	245	85
1200-1500	406	65	416	89
1500 and over	66	62	72	83
Total	967*	59	1006	83

*Definite information regarding menopausal symptoms could not be obtained in every case followed up.

Table IX shows the infrequency with which unfavorable complications or recurrences were encountered in the 300 patients in this series ten years or more after they had been irradiated.

TABLE IX. RECURRENCES OR COMPLICATIONS OCCURRING TEN YEARS OR MORE AFTER IRRADIATION

DIAGNOSIS	NUMBER OF PATIENTS FOLLOWED UP 10 YEARS OR MORE	RECURRENCES OF COMPLICATIONS	
		NUMBER	PER CENT
Functional hemorrhage	116	5	4
Myoma uteri	184	4	2
Combined total	300	9	3

Table X summarizes briefly the results secured in those cases of functional hemorrhage in which one irradiation failed to produce satisfactory results, together with the final outcome.

TABLE X. UNSATISFACTORY RESULTS FOLLOWING ONE IRRADIATION FOR FUNCTIONAL HEMORRHAGE; SUBSEQUENT TREATMENT; FINAL RESULT

INITIAL TREATMENT UNSATISFACTORY RESULT NUMBER OF PATIENTS	SUBSEQUENT TREATMENT	FINAL RESULT SATISFACTORY NUMBER OF PATIENTS
49	Reirradiation	49
17	Hysterectomy	14
5	Pelvic surgery	5
12	Hormone therapy	12
3	Not stated	3
6	No treatment	0
Total 92		83

Table XI shows the final outcome among the cases of uterine myoma in which one irradiation failed to secure satisfactory results.

TABLE XI. UNSATISFACTORY RESULTS FOLLOWING ONE IRRADIATION FOR MYOMA UTERI; SUBSEQUENT TREATMENT; FINAL RESULT

INITIAL TREATMENT UNSATISFACTORY RESULT NUMBER OF PATIENTS	SUBSEQUENT TREATMENT	FINAL RESULT SATISFACTORY NUMBER OF PATIENTS
37	Reirradiation	37
31	Hysterectomy	30
3	Myomectomy	2
1	Oophorectomy	0
1	Exploratory	0
1	No treatment	0
Total 74		69

TABLE XII. PELVIC CARCINOMA DEVELOPING IN PATIENTS AFTER IRRADIATION FOR FUNCTIONAL HEMORRHAGE AND MYOMA UTERI

DIAGNOSIS	PATIENTS IRRADIATED NUMBER	PELVIC CARCINOMA NUMBER
Functional hemorrhage	521	4
Myoma uteri	485	7
Total	1006	11
Extrapelvic carcinoma developed in 5 additional patients		

TABLE XIII. OPERATIVE MORTALITY—ENTIRE SERIES

DIAGNOSIS	NUMBER OF PATIENTS	NUMBER OF DEATHS	MORTALITY PER CENT
Functional hemorrhage	750	1*	0.13
Myoma uteri	687	3†	0.4
Total	1437	4	0.278

Causes of Death: **Vincent's Angina* seven days after irradiation.

†1. *Pneumococcal Meningitis* on the third day. This patient had an ulcer of the nasal septum on admission. 2, *Cerebral hemorrhage* on the fifth day. 3. *Intestinal Obstruction* on the tenth day.

CONCLUSIONS

1. To secure good results from irradiation, the cases must be carefully selected; this requires not only correct judgment, but diagnostic and histologic skill.

2. The destructive effects of irradiation, while being the direct means by which the hemorrhage is checked, also constitute a definite drawback to this form of treatment.

3. In a study of 1,437 cases of benign hemorrhage treated by means of intrauterine radium irradiation, 750 were cases of functional hemorrhage, and 687 of myomas. One thousand and six patients of the

entire series were followed up for two years or more, and 300 of these patients have been observed over a period varying from ten to twenty years.

4. Menopausal symptoms occurred in 59 per cent of 967 reported cases of functional hemorrhage and myomas.

5. Satisfactory results were secured in 83 per cent of the group of cases.

6. The myoma cases yielded about the same proportion of satisfactory results as did the functional hemorrhage cases.

7. Three per cent developed relapses or complications requiring treatment ten or more years after irradiation.

8. The proportion of cases in the followed-up group in which carcinoma of the genital tract developed after irradiation was 1.09 per cent.

9. The mortality in the entire group was 4 patients or 0.278 per cent.

133 SOUTH THIRTY-SIXTH STREET

DISCUSSION

DR. JAMES E. KING, BUFFALO, N. Y.—In this series presented I am sure that many will feel that ovarian function has been destroyed too often. I believe it is a mistake to induce the menopausal symptoms in women under forty. I have always found it far simpler to explain to a young woman why her abnormal bleeding returns than to console her after the induction of a premature menopause.

My own practice has been to use small doses of radium in women under forty, and the larger doses in women past forty-five. In the former one can only regard the treatment as palliative and in about 30 per cent of these cases subsequent treatment will be required.

From 1922 to 1936, a fourteen-year period, I personally irradiated 226 fibroids. Approximately 70 per cent of these were associated with hyperplasia. In the remaining 30 per cent, the scrapings were reported as premenstrual swelling or in the absence of tissue they were regarded as an atrophic endometrium. There is little definite knowledge as yet to justify a diagnosis of "endocrine bleeding."

During the past three years in three of my patients irradiated for benign bleeding a subsequent pregnancy required cesarean section for dystocia due to the failure of the lower uterine segment to dilate. In one case the uterus was removed and the pathologist reported the condition as being due to cicatricial tissue. Following these cases the radium was packed high into the fundus.

I have a few slides showing the results of irradiating 114 fibroids in the five-year period from 1927 to 1931. It was possible to follow 104 of these cases. Of these 104 cases, 85, or 81 per cent, were "cured" either by a correction of the abnormal bleeding or in the older patients by the production of the menopause. Four of these 104 patients have had labors at term. Fourteen of the 104 were subsequently advised to have an operation. Ten hysterectomies were done, one large submucous polyp was removed and three refused surgery.

Hyperplasia was found in 71 per cent of the 114 cases. This large percentage strongly suggests a definite relationship between fibroids and endometrial hyperplasia, and very possibly the same etiologic factor is concerned in the production of both.

DR. FRANK A. PEMBERTON, BOSTON, MASS.—We have treated only 90 fibroids with radium because my former chief, Dr. Graves, thought that operation was better on the whole than radium. I am going to confine my discussion to cases of functional bleeding.

We have treated 762 patients and have been able to follow 425, or 55 per cent, two or more years. We have divided them into two groups. In one we did not want to cause change of life, while in the other group we did wish to. In the first group are 131 patients, 14 per cent of whom are under twenty years of age, 31 per cent between twenty and twenty-nine, 50 per cent between thirty and thirty-nine. In the group where we wanted to cause change of life there were no patients under twenty, only one up to thirty, 18 per cent between thirty and thirty-nine, and the great majority over forty.

Among the 131 patients in whom we did not want to cause change of life, 86 were regarded as cured, 8 were relieved to the extent that their profuse flowing stopped, but they had irregular periods, and 8 required another radium treatment. In this group of cases we used from 200 to 500 mg. hours, rarely more than 400 mg. hours. Four, all thirty years old or over, we count as failures because we caused amenorrhea. Seventy-eight per cent of this group gave satisfactory results, which is about the same as Behney's. In 13 patients we had to use secondary treatment as follows: hysterectomy, 6; radium to cause the menopause, 6; and x-ray treatment, 1. The other 12 out of the total went elsewhere for further treatment.

The second group consisted of 294 patients. One (0.3 per cent) was under thirty years of age and only 56 (18.7 per cent) were under forty. The results were satisfactory in 283 (96 per cent). The dosage varied from 800 to 1,600 mg. hours with a few of 2,400. Secondary treatment was required in the other 11 and consisted of hysterectomy in 8 and more radiation in 3.

In the first group of 131 cases there were 35 pregnancies among 24 patients. These occurred in patients who had normal periods following only one radium treatment. They had 20 normal babies, 7 stillbirths, and 9 miscarriages, which I think again agrees approximately with Behney's figures.

We follow the same indications for treatment that Behney uses. As regards the symptoms of menopause, we feel that they are about the same as those following operation. They are more likely to be severe in nervous and highly strung women, and therefore we operate on such patients and conserve an ovary. These represent, however, a small percentage of all cases.

There were 4 patients out of 425 who developed intrapelvic tumors after treatment. One was a twenty-six-year-old woman who was admitted to another hospital six years later for an inoperable pelvic tumor, the character of which was not determined. The second was a thirty-six-year-old woman. She was discovered by a survey of the death records at the State House to have died, six years after our treatment, of cancer of the cervix. It is very possible that she had cervical cancer at the time we treated her, but it was so small that we missed it. The third patient was found to have a cancer of the endometrium eleven years after our treatment, and the fourth, a forty-six-year-old woman, died of general abdominal carcinomatosis, probably originating in the ovary, fifteen years after our treatment. We do not feel responsible for any of these except possibly the second one.

DR. WALTER T. DANNREUTHER, NEW YORK, N. Y.—I can refer only to a modest series of 183 patients treated personally during a thirteen-year period. In the main, the results in this small group do not differ materially from those reported by Behney. He has truly stated that the cases must be carefully selected, and has outlined the contraindications for radium therapy, which conform with the prevailing opinion of most gynecologists.

It would also be of interest to know the number of patients in whom menstruation was reestablished after the irradiation. The preservation of the menstrual function, together with 31 pregnancies eventuating in 15 living children, would seem to cast some doubt on the statement that "the success of the treatment is dependent largely, if not entirely, on the inhibiting or destructive action of the irradiation on the ovarian endocrine system." The contraction of fibromyomas and the fibrosis of the myometrium following irradiation, with the continuation of menstruation in so many cases, can justly be regarded as additional evidence that there is at least some local effect on the uterus which contributes to the arrest of the normal bleeding.

The inclusion of 15 patients less than twenty-one years of age is somewhat surprising, as the treatment of the bleeding of puberty or adolescence can nearly always be satisfactorily controlled by other methods.

My experience has been that about 18 per cent of white patients with fibroids requiring treatment are suitable candidates for radium therapy; that the menstrual function will be preserved in 78 per cent of cases when the dose is 750 mg. hours or less; and that in 13 per cent of cases it has a depressing effect on sexual inclinations. There have been 6 pregnancies in 4 of my 183 patients, resulting in 4 living children. There has been no mortality.

DR. EARDLEY HOLLAND, LONDON, ENGLAND.—Many of the climacteric cases have leucorrhoea after radiation, but we have been able to diminish the incidence of this a great deal by careful secondary screenage of the platinum retainer which we think has an atrophic effect on the endometrium.

An important question is whether radium in the uterus has any effect in increasing the incidence of cancer of the body of the uterus. There are some authors who believe that. I do not believe that there is any connection, but it must be definitely settled one way or the other.

It is also important to make a most careful investigation in every case of functional hemorrhage. Every patient should have a complete blood examination, including coagulation time, bleeding time, and metabolic rate. Otherwise we shall find ourselves producing a menopause in patients who have nothing more than hypothyroidism. Years ago I introduced radium into the uterus of a girl of twenty-one because she had formerly had an attack of bleeding which finally had been stopped. She was ultimately cured of purpura by splenectomy.

Some patients are very vague in reporting menstrual histories, and we found it very difficult to get a good record of uterine hemorrhage. I have therefore devised some graphic uterine hemorrhage charts which I have used for my students who find them of enormous help. This is a chart I use in all cases where there is a history of regular menstruation. It is divided into months and shows the days up to 31. If the patient has what we call spotting of blood, it is shown by a little spot; average menstruation is shown by one square; a show of blood is indicated by a little streak; excessive bleeding is shown by two squares; flooding, by three squares. Of course, these do not pretend to be accurate measurements but it simply gives a graphic history.

For example, here is shown a patient's history recorded in this way. She was a woman of fifty-two with climacteric hemorrhage, who came to me having had normal periods in November and in December, and then another so-called period three days after that. She menstruated perfectly normally for the next few months and then her doctor brought her in again because she had had a normal period, a prolonged period, and then severe bleeding. Since her hemoglobin was only 26 per cent, she was given a blood transfusion, a radium treatment, and Bland's pills. Her hemoglobin went up to 80 per cent and she is now perfectly well.

May I suggest that if you take your histories in this way you will have a graphic account of the patient and your students will appreciate it immensely. Those of you who are in the habit of giving hormone treatment will find it very useful for such recording.

DR. NORRIS (closing).—An endeavor has been made in this paper to point out that irradiation is not an ideal treatment, although it is believed the best for certain types of cases. Certainly the functional cases should, at least theoretically, be treated along the lines of endocrine therapy. It is now routine with us to attempt conservative treatment, which includes endocrine therapy, in all women suffering from functional uterine hemorrhage who are in the childbearing age. Irradiation is advised only after these methods have failed.

I had thought before our follow-up was completed that we would find results in the myoma cases not as satisfactory as in a corresponding group of the functional cases, but as a matter of fact all through this series it was about the same. I think we irradiate perhaps one case in five where a symptom-producing myoma is present.

The condition of the postradiated endometrium is a subject which has interested me very much. I have personally examined perhaps 50 uteri, in which there have been irradiation six months or more previously, and have yet to see a case where there was any gross pathologic evidence of the treatment. I have sectioned most of these uteri and in only one or two have I been able to see anything under the microscope that indicated previous irradiation, other than senile changes which were general throughout the endometrium. Theoretically I think there must be some scar tissue due to irradiation, but it plays no part in the final result.

There are two prices which the woman who is subjected to irradiation instead of operation pays. One of them is that a certain proportion will suffer from discharge for about six weeks, sometimes for three months, and sometimes a little longer. That is one minor drawback. The other is that the patient will have to return regularly for a follow-up for a prolonged period of time. This is particularly true in the myoma group, where the tumor is still present after treatment, and we do not know exactly what may happen to it.

It is hard to determine the proportion of carcinoma which developed in this series, and whether or not it is out of proportion to the normal carcinoma incidence. We all feel, I think, that chronic irritation plays a part in the predisposition to carcinoma. After irradiation there is chronic irritation but for a relatively short time only. Another factor is that irradiation patients have a longer cancer age, since it is probably the sex age of the individual which is a predisposing factor to cancer rather than the actual age in years.

Perez and Arenas: *Myiasis of the Vulva*, Bol. Soc. de obst. y Ginec. (Buenos Aires) 14: 849, 1935.

The authors report 2 cases of myiasis of the vulva. The rarity of finding the larvae of the fly in this location they feel is due to the natural protection of these parts. It is not rare to find myiasis of the auditory canal, nares, etc.

In both cases there was localized swelling of the labia, and a canalization of the skin, from openings of which from 8 to 10 larvae were extracted. The treatment consisted in washing out the cavities with chloroform water and applications of thymol into the cavities. Both patients were cured in about ten days. The authors find only 4 other cases reported in the literature.

MARIO A. CASTALLO.

RELATION OF ENDOMETRIAL HYPERPLASIA TO ADENOCARCINOMA OF THE UTERUS

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IN THE overwhelming majority of cases, hyperplasia of the endometrium is, from a pathologic standpoint, a frankly benign lesion. In a small minority of cases, however, it presents proliferative features which tax the judgment of the pathologist who is called upon to decide whether or not they are indicative of malignancy. With most of these borderline pictures, one who is familiar with the proliferative vagaries of hyperplasia will usually, though not always, decide against actual cancer; but the further question arises as to whether a lesion which can present such cancer-like features may not at times step over the line and give rise to genuine cancer—whether, in other words, it is not to be looked upon as a precancerous lesion, in the usual sense of that much-abused but not unuseful term, i.e., as indicating a lesion which predisposes to cancer rather than one which represents a transition from benign to cancerous disease.

It is with this general problem in mind that we have recently re-studied all the cases of endometrial hyperplasia and of adenocarcinoma of the uterine body which have passed through our laboratory during the past eleven years. During this period, a total of 12,813 case specimens has been reviewed. Among these we have encountered 804 cases of endometrial hyperplasia and 104 of corporeal adenocarcinoma. With the hyperplasia cases we have been chiefly concerned in sifting out those in which there has been evidence of unusual proliferative activity, producing pictures which histologically would seem to constitute varying degrees of approach to that of cancer itself. In the adenocarcinoma group the natural plan of such a study as ours, and the one which we have followed, is to determine how frequently cancer has occurred in uteri showing also hyperplasia, and how frequently the antecedence of hyperplasia is indicated by previous histological studies or by the clinical history.

Until recent years most authors have been inclined to deny to hyperplasia any such predisposing influence in the development of cancer; as, for example, many have ascribed to such lesions as leucoplakia of the cervix, cervical irritation or erosion, Schimmelbusch's disease of the breast, or gastric ulcer, and certainly far less than to leucoplakia of

*Dr. Yui's part in this work was made possible by the Mary Putnam Jacob Fellowship of the Women's Medical Association of New York City.

the vulva. This was formerly the view held in our own laboratory, as expressed in the paper of Novak and Martzloff in 1924, and in several other publications both before and after this. Similar opinions have been expressed by numerous other writers (Schröder, Shaw, Cullen, Burch). In the most recent paper on the subject, L. E. Burch states that "I have never seen the two conditions associated together in the same patient, nor have I ever seen hyperplasia as a forerunner to cancer."

A number of authors (Meyer, Schröder, Taylor) have reported cases in which adenocarcinoma had developed in uteri which were the seat of hyperplasia; and we had likewise occasionally observed this association without attaching great significance to it. Both these lesions are so common that it would seem strange if they did not occasionally co-exist, and in the past we have felt that this factor of coincidence explained cases in which both lesions existed side by side, rather than any more fundamental relationship between the two.

The studies of Mack and others have seemed to indicate that the clinical severity of the symptoms with hyperplasia parallels the degree of proliferative activity. For example, the cases of "mild" hyperplasia in his 200 series of cases were often cured by curettage alone, while in the severe grades, recurrence of bleeding was the rule, with cure only by the induction of the menopause by x-ray or radium. More important, however, have been the occasional reports of cases in which areas of unquestioned carcinoma have been found developing in a hyperplastic endometrium. In 1923 Meyer described two cases in which islands of undoubted adenocarcinoma were found embedded in the hyperplastic endometrium, much like implanted ova, and in one of these a direct transition from the benign to the cancerous areas was demonstrable.

This author has consistently expressed the viewpoint that all gradations between frankly benign and obviously malignant lesions may be seen, though, like all others, he emphasizes the fact that in the vast majority of cases, hyperplasia presents no great difficulty of microscopic diagnosis because of the complete absence of any suspicious histologic malignancy. In a small group of cases, however, the problem is far more difficult. Lesions closely simulating cancer, and yet proved by their subsequent clinical course to be benign, may be encountered, and so may actual cancer, on the basis of both histologic and clinical criteria.

Even expert pathologists will disagree in the interpretation of a certain small proportion of cases; and a careful follow-up study of a large number of borderline cases which have received only very conservative treatment, usually nothing more than curettage, is necessary to justify the histologic assumption of nonmalignancy. After all, it is what happens to the patient who is untreated, or treated only by conservative measures not capable of curing cancer, that determines

whether or not a lesion is malignant. Viewed in this light malignancy is fundamentally a clinical and not a histologic attribute, although by years of correlative study pathologists have learned to recognize certain histologic criteria as going hand-in-hand with clinical malignancy.

Only a few follow-up studies of these borderline lesions have been made. In Meyer's laboratory Hintze has studied 24 cases diagnosed as benign, but presenting such marked glandular and epithelial changes that they would certainly be interpreted by many as indicative of cancer. Although the only operation carried out in these cases was diagnostic curettage, not one of them subsequently developed cancer, a flattering tribute to the diagnostic acumen characterizing this laboratory.

An excellent study of the relation of hyperplasia to adenocarcinoma was made in 1932 by Taylor, whose material included 85 cases of hyperplasia, 50 of cervical polyps, and 152 of adenocarcinoma. This author presented evidence, available chiefly from the adenocarcinoma cases, that hyperplasia may be a predisposing factor in the later development of cancer.

Within recent years, we have been more and more impressed with the fact that hyperplasia is not so devoid of harmful possibilities as we once thought; or, to put it more accurately, that the proliferative forces responsible for benign hyperplasia may predispose to the development of cancer. The more and more frequent finding of borderline pictures; the increasing observation of cases in which hyperplasia and adenocarcinoma coexist, with at times apparently gradual transition of one into the other; the occasional occurrence of a history of functional menopausal bleeding and hyperplasia in patients who later develop adenocarcinoma—all these must make us question the innocuousness of hyperplasia. A further incentive for the present investigation of the subject is given by the recent studies which indicate that certain estrogenic substances are carcinogenic, so that it would not be surprising, to say the least, if a lesion known to be due to an excessive and prolonged estrin stimulation might predispose to cancer even more than merely irritative lesions, to which such a predisposing rôle is rather generally ascribed.

This is not the place to discuss the characteristics of benign hyperplasia, which are familiar to all gynecologic pathologists. It should be stressed, however, that the histologic picture is not a constant one, and that the same underlying process is concerned whether the endometrium presents the "Swiss-cheese" pattern, or a pattern scarcely distinguishable from that of the normal-interval endometrium, or a markedly proliferative pattern characterized by adenomatous activity of the glands and stratification of the epithelium. The term hyperplasia, therefore, as we have many times stressed, is a rather loose and not an altogether satisfactory one; but it is now so well established that it would not be easy to dislodge it. The proper evaluation of the histologic variations of hyperplasia can be made only if one bears in mind that they represent merely the reaction of the endometrium to varying degrees of estrin stimulation, and that there is an insensible

gradation from the normal proliferative or interval type of endometrium, to the so-called mild hyperplasia, then to the hyperplasia of frank "Swiss-cheese" pattern, and finally to the markedly proliferative hyperplasia pictures which may even closely resemble cancer.

The question then naturally suggests itself as to whether the next step might not be into the domain of actual cancer. As already stated, this possibility does not seem so remote in view of the newer work on the relation of endoerines, and especially the estrogenic substances, to cancer. The old dictum that a lesion is either cancer or not cancer may still be true; but there are many histologic intergrades which often make the decision difficult or impossible, though it cannot be assumed that in such cases we are actually witnessing a transition of benign into malignant disease.

As has been stated, the histologic picture characterizing hyperplasia of the endometrium, varied though it is, is not in any way suggestive of malignancy except in a very small proportion of cases. On the other hand, it is not so rare to find moderate degrees of proliferative overactivity, and it is possible, in the study of any large group, to demonstrate a definite gradation of changes from the frankly benign to the frankly malignant. Indeed, in one and the same uterus, as we shall show, one may see what is apparently a transition from a very benign type of hyperplasia, to areas which must be classed as borderline, and then to what all pathologists would agree is actual cancer. This statement cannot be made of cancer in most other regions, in which the demarcation between the cancerous and noncancerous tissue is likely to be quite sharp. Nor, it should be added, is it by any means true of all cases of corporeal adenocarcinoma. Hence, the special interest of hyperplasia in relation to cancer, an interest doubled by its estrogenic etiology, and by the newly demonstrated relations between estrogenic and carcinogenic substances.

In the milder degrees of departure from the typical benign "Swiss-cheese" pattern so common in hyperplasia, one may find only an unusual degree of epithelial proliferative activity, evidenced by pseudostratification or actual stratification, most frequently in the smaller glands. The epithelial nuclei may be larger and may take a much heavier stain than normal, while the glands themselves may be closely placed, so that the questionable area stands out quite sharply from its surroundings. In other instances, it is the paler staining of the questionable area which, as in many cases of actual cancer, sets it out in relief to the surrounding tissue. Mitotic activity, so characteristic of hyperplasia in general, is of little value in the differential diagnosis between this condition and adenocarcinoma. Occasionally, as in Fig. 4, the epithelium of the glands may exhibit what is apparently a definitely metaplastic change, so that it resembles quite perfectly the



Fig. 1.



Fig. 2.

Fig. 1.—(Gyn. Path. No. 33193.) Showing mild proliferative activity in some of the smaller glands, with no suggestion of malignancy. Patient, aged forty-five years, had had persistent bleeding for four months.

Fig. 2.—(Gyn. Path. No. 41075.) Adenoma-like area in a case of benign hyperplasia. Patient, aged forty-one years, had had menorrhagia and metrorrhagia for one year.



Fig. 3.



Fig. 4.

Fig. 3.—(Gyn. Path. No. 36587.) Markedly atypical gland pattern in benign hyperplasia. Patient, aged fifty years, was curetted five and a half years ago, and has remained perfectly well with no other treatment.

Fig. 4.—(Gyn. Path. No. 34478.) Such an area as this, which by its paler staining and the unusual epithelial changes, stands out from the surrounding tissue, might well lead to the suspicion of cancer. The epithelium in many places resembles that of the tube.

epithelium of the fallopian tube. The occurrence and significance of this metaplasia have been discussed in a previous paper by one of us (Novak).

In other cases, the glands themselves may show marked increase in number, with almost no interglandular tissue, and perhaps with very atypical convolutions and involutions. It is easy to see how such a picture, coupled with such epithelial overactivity as has been described in the preceding paragraph, must make the pathologist pause, and how one not familiar with the vagaries of hyperplasia might suspect adenocarcinoma. As a matter of fact, even expert pathologists will disagree in the interpretation of certain cases.

Since these perplexing problems most frequently arise in the diagnosis of uterine scrapings obtained by diagnostic curettage, their momentous bearing upon the patients' welfare is obvious, with a therapeutic decision to be made between simple radiotherapy and radical operation. No wonder, therefore, that in the occasional case the decision will be that of an eminent foreign gynecologist, also an excellent pathologist, who, on examining such a doubtful section in our laboratory during a recent visit, gave as his verdict, "Nicht Karzinom, aber besser heraus."

In only 13 of our patients during the reproductive epoch have we encountered such noteworthy evidences of proliferative activity as to raise the question of possible malignancy, though in all of these the changes involved only localized areas. The examination of the histologic context and the clinical histories of the patients made the exclusion of cancer reasonably easy and safe, and in no case was this diagnosis belied by the subsequent history. It will be seen, therefore, that in only a very small percentage of cases (1.3 per cent in our series) does the common hyperplasia of the reproductive epoch present pictures which might lead to the suspicion of cancer. The vast majority of cases are, from a histologic standpoint, very frankly benign.

Aside from such cancer-like areas as have been described, we have been interested in a rather curious epithelial reaction which we have noted in two of our cases. This is illustrated in Figs. 5 and 6. This epithelial change, which is seen only in scattered areas, is characterized by marked stratification, with often a synectial merging of the cells of either the surface or gland epithelium. The cells become large and often develop vacuoles which may become so large that by compression of surrounding cells they produce a pseudoglandular picture. The synectial suggestion is accentuated by the fact that the basement membrane is blurred and appears at times to be completely lost. An interesting feature is the infiltration with many eosinophilic leucocytes, while mitosis may likewise be noted.

We have been all the more interested in this picture because of its exact similarity with that recently produced experimentally by Migliavacca by injections of estrin into rats which had been previously eas-

trated. The effects produced upon the endometrium by employing this technic were interpreted by Migliavacca as due, not alone to estrin, but also to the prolan A normally found in castrated animals. In other



Fig. 5.

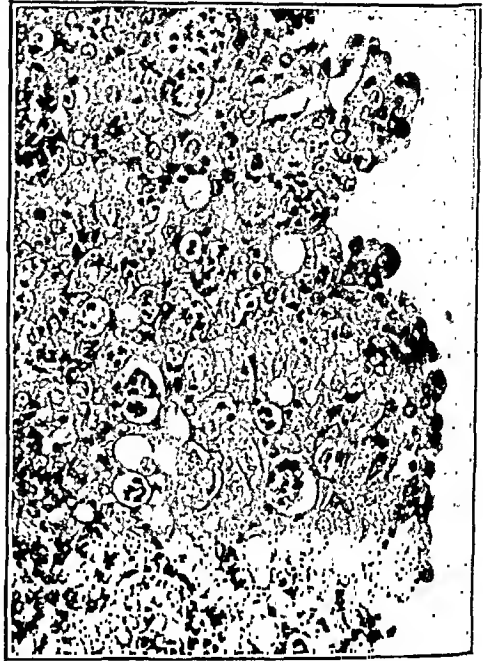


Fig. 6.

Fig. 5.—(Gyn. Path. No. 41075.) An area of peculiar "syncytial" proliferation of epithelium in the same case of hyperplasia from which Fig. 2 is taken.

Fig. 6.—(Gyn. Path. 37089.) Another syncytium-like picture, with somewhat higher power than that used in Fig. 5, from a patient of fifty-five years who had had irregular bleeding for five months. Other parts of the section show typical benign hyperplasia, and she has remained well after curettage five years ago.

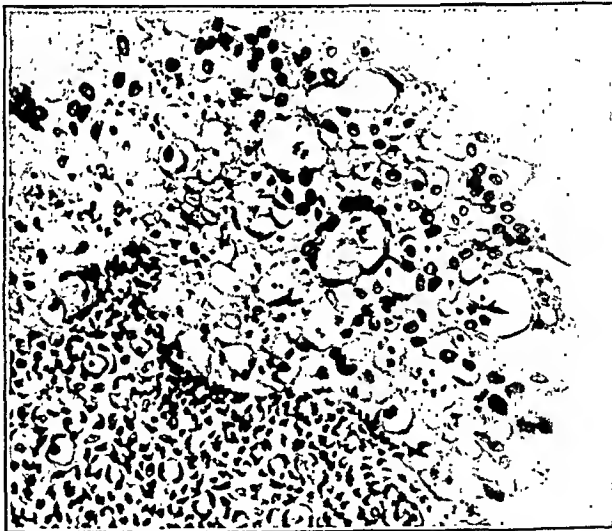


Fig. 7.—Syncytium-like epithelial proliferation produced by estrin injections into castrated rabbits (combined effect of estrin and Prolan A?). (Migliavacca.) Compare with Figs. 5 and 6.

words, he feels that these syncytium-like epithelial changes are to be explained as due to the combined action of these two hormone principles; and it is possible that the same explanation may apply to the

closely similar changes seen in our two cases. We had never previously observed such epithelial changes, and, so far as we know, they have not previously been noted in the human endometrium. Just why they should have manifested themselves in these two cases we do not know, as there seem to be no distinctive features in the histories of these two patients.

Another interesting epithelial change which we have encountered in six of our cases is the so-called squamous metaplasia. This is a relatively infrequent finding, though it has been described by a number of authors (Polano, Engelhorn, Novak). It may involve either the surface epithelium or that of the glands, more commonly the latter.



Fig. 8.—(Gyn. Path. No. 33712.) Squamous metaplasia of surface epithelium in a case of hyperplasia. Similar metaplastic changes were found in the gland epithelium of the same case. Patient aged twenty-eight years.

Meyer states that most characteristically the squamous nests project into the gland lumen in a glomerulus-like fashion. This is well illustrated in one of our cases (Fig. 8). Frequently, too, where the hyperplastic endometrium invades the musculature, the metaplastic changes are quite striking in the invading glands, producing complex patterns which may well lead to the suspicion of malignancy (Fig. 9).

There has been much discussion as to the mechanism of this squamous "metaplasia" since the first description of the condition by Ruge and Veit, as far back as 1882. It is seen in most extensive degree in association with the form of endometrial cancer designated as adenocan-

eroid or adenoacanthoma; and there has been considerable discussion as to whether the cancer arises from a double matrix ("Doppeltumor"



Fig. 9.—(Gyn. Path. No. 32156.) Squamous cell metaplasia in the glands penetrating the uterine musculature, the mucosa generally showing frankly benign hyperplasia.

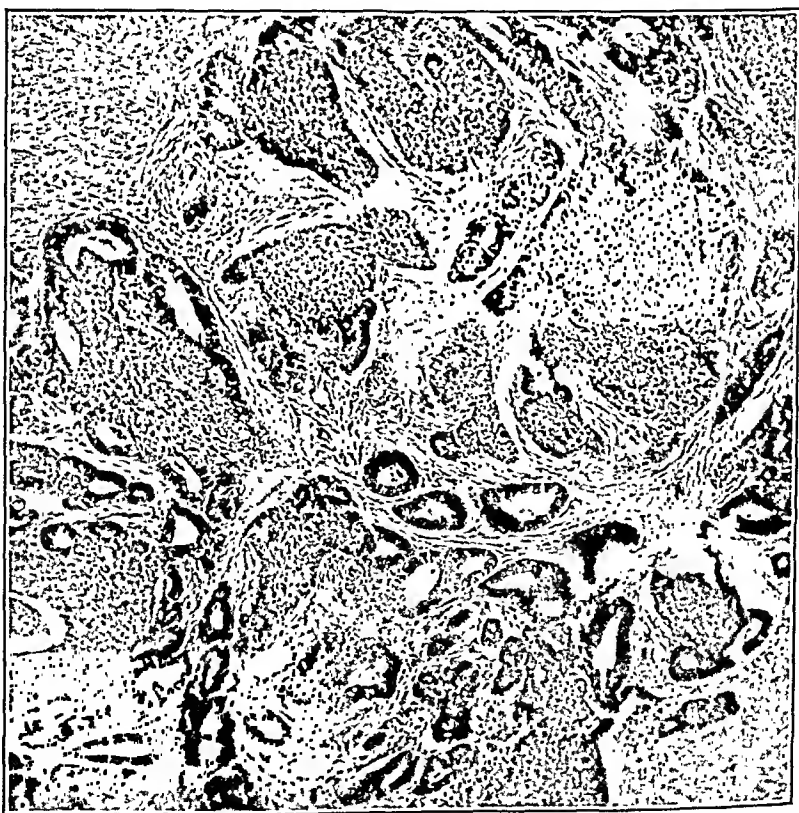


Fig. 10.—Extensive squamous metaplasia associated with adenocarcinoma, the interglandular squamous epithelium showing no histological evidence of malignancy.

or "Collisionstumor"), or whether the squamous transformation is a later development in an adenocarcinoma. The latter viewpoint is the one which seems to have achieved the widest acceptance. Usually the

squamous epithelial growth is a benign concomitant of the malignant cylindric-cell carcinoma, but it may at times assume malignant characteristics of its own. The squamous epithelium probably arises from undifferentiated cells beneath the cylindric epithelium, cells which, under appropriate stimulation, may develop into squamous epithelium.

The most remarkable instance of this metaplastic change which we have observed is illustrated in Fig. 10, from a case of adenocarcinoma. In this section the squamous metaplastic areas have practically replaced the stroma and in many places seem to be compressing the gland structures. In this unusual picture the interglandular squamous epithelium shows no histologic evidence of malignancy, though it would seem that its obviously active growth propensities would make the step toward actual cancer a rather short one.

A special word seems necessary as to the striking pseudomalignant proliferative changes which one not infrequently sees in the polyps which so often are seen in cases of hyperplasia. This applies more particularly to the multiple polyposis of marked hyperplasia rather than to the single polyps of stationary hyperplasia pattern which may be found even when the endometrium as a whole is of the normal functioning type. The latter represent one type of so-called localized hyperplasia, corresponding to the localized areas of hyperplasia or "unripe endometrium" which may be found at various levels in the endometrium proper.

In a paper published by Novak and Martzloff from this laboratory some years ago (1924), attention was called to the fact that in polypoid hyperplasia the glands in the polyps may be so closely packed, and proliferative changes so marked, as to simulate adenocarcinoma very closely. Indeed, if such changes were seen in the endometrium proper, this diagnosis would no doubt be made by many pathologists; and yet their significance in polyps is much less. Actual carcinomatous changes can of course occur in uterine polyps, but they are relatively rare. Of the cases which have been reported, some at least are cases of polypoid carcinoma, for adenocarcinoma occasionally begins in just this polypoid form. It is especially this type in which, in a considerable number of reported cases, complete removal has apparently been accomplished by the curette, the microscopic examination of the uterus after removal showing no evidence of cancer. The examination of the pedicle is of great importance in deciding whether one is dealing with a polypoid cancer or a benign polyp which has undergone malignant change. The latter assumption is justified if there is no trace of cancer in the pedicle.

While this paper is primarily concerned with the gradations of epithelial proliferation seen in hyperplasia and adenocarcinoma, it is of interest to note that in an occasional instance it is the stromal elements which appear to bear the brunt of the proliferative forces at play in hyperplasia, and that in its most extreme form apparently tend to

the development of actual sarcoma of endometrial origin. The most striking instance of this kind which we have observed occurred in a patient of twenty-eight, who had had two eurettements for persistent uterine bleeding, the scrapings showing typical hyperplasia, with also areas of epidermization, as shown in Fig. 8. The endometrium in the last euretting showed rather striking stromal activity, with an unusual number of mitoses and at least some nuclear hyperchromatosis. One year later she died in another city, and autopsy tissue which was received in our laboratory showed indubitable and extensive sarcoma of the endometrium.

One of the most surprising developments of this study is the finding of what is apparently a perfectly typical and actively growing hyperplasia in women often far beyond the menopause. The general view has always been that hyperplasia is a disease of reproductive life, though it may be observed for at least a short time after the actual cessation of menstrual function, in conformity with the existence of hyperestrinism during the earlier phases of the menopause (Zondek). Without having made any chronologic studies on this point, we ourselves have in past years thought it unlikely that hyperplasia could persist for more than a year or two after the cessation of menstruation, except in relatively rare cases in which a granulosa-cell tumor of the ovary is present.

And yet, in the study of this large material, we have found no less than 40 cases in which typical hyperplasia is found present in women from one to twenty-four years after the last menstrual period. In 32 of these 40 cases in which the data as to age are accurate, more than one year had elapsed since the menopause (two years in 4, three years in 2, four years in 2, 7 years in 4, eight years in 1, nine years in 2, ten years in 2, fifteen years in 3, sixteen years in 4, eighteen years in 1, nineteen years in 2, twenty years in 1, twenty-two years in 3, and twenty-four years in 1). In the remaining 8 cases, the patients were within one year of the menopause.

The histologic diagnosis in these cases we believe to be unimpeachable. It was of course not made on the mere basis of such features as large, cystic glands, as these are quite common in the senile endometrium. But when one finds the typical "swiss-cheese" pattern, with active epithelial growth, and an abundance of dense stroma not distinguishable from that of the reproductive phase, no other histologic diagnosis is possible. We are confident that if the age of the patient were not known, such a picture as that represented in Fig. 11, representing the endometrium of a woman of seventy-five years, would at once be diagnosed by every pathologist as typical hyperplasia.

The fact that hyperplasia may thus be found in women long after the menopause lessens the significance of this lesion in relation to granulosa-cell ovarian carcinoma of elderly women, in whom this ovarian tumor, as is well known, rather characteristically brings about an apparent

reestablishment of menstrual bleeding. Examination of the uterine mucosa in such cases usually reveals hyperplasia. Both the bleeding and the hyperplasia are explainable as due to the estrin produced by the ovarian tumor, so that it has commonly been accepted that the finding of well-marked hyperplasia in postmenopausal women should make one suspicious of granulosa-cell carcinoma. This is still true, but, unless one can also palpate an ovarian tumor, one is certainly not justified in assuming that a small nonpalpable granulosa-cell carcinoma probably exists, as some of us formerly believed.

It has been quite clearly established, both in the human being and in the experimental animal, that the immediate cause of hyperplasia is an excessive stimulation with estrin, underlying which is an overactivity of the follicle-ripening gonadotropic hormone of the anterior hypophyseal lobe. What, then, is the source of the estrin in this late post-

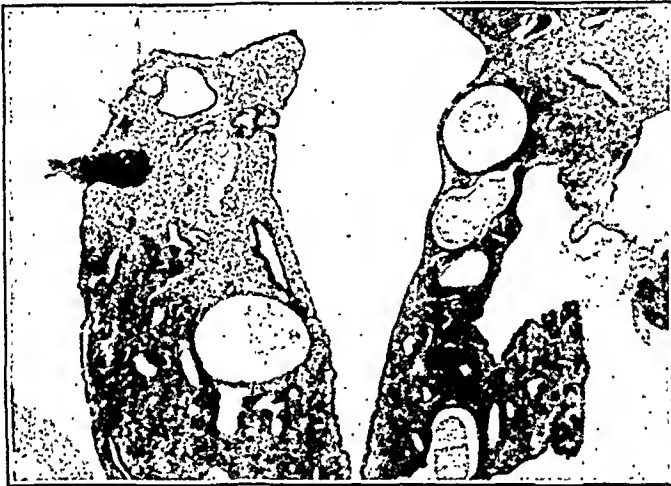


Fig. 11.—(Gyn. Path. No. 41389.) Benign hyperplasia from a patient of seventy-five years, twenty years after the menopause. There had been sudden profuse bleeding beginning four days before admission.

menopausal or senile phase of life, long after cessation of ovarian secretory activity? That the ovaries have actually become functionless receives histologic support in 19 of our cases in which they are available for study. They present the typical senile structure, with no sign of follicular activity and in some cases with practically complete disappearance of all follicular structures. Estrin has been found in the urine of women long after the menopause, though no intensive studies on this point appear to have been made. It is difficult to believe that the source of the hormone can be the senile ovary, and it seems more likely that some other structure, possibly the anterior pituitary lobe, may assume an estrogenic function when the ovary steps out of this rôle. We expect to be able, by hormone studies now being projected in our laboratory, to throw some light on this question of estrin production in old women, and perhaps thus on the occasional occurrence of hyperplasia in postmenopausal life.

Frank has, in several publications, mentioned finding the estrogenic factor in the urine of women after the menopause, although he does not discuss the source of the hormone in these cases. Especially suggestive, however, is the recent paper by Frank, Goldberger and Salmon, in which report is made of the finding of the estrogenic factor in the urine of surgically castrated women. This would at once seem to indicate that the ovaries are not the producing source, a view coinciding with our own impressions, based on the less decisive histologic studies we have been able to make of the ovaries of women with postmenopausal hyperplasia.

In a recent study of 130 cases of postmenopausal bleeding, all in women over forty-five who had had complete amenorrhea for from one year to twenty-five years, Breipohl reports the finding of a proliferative endometrium in 13, hyperplasia in 15 (this including 2 in which there was a granulosa tumor of the ovary), secretory endometrium in 3. In other words, in 31 of 130 bleeding cases, almost 25 per cent, the endometrium exhibited evidence of undoubted activity, though menstruation had ceased long before. Nearly half of this group was made up of cases of hyperplasia, which in one case was observed as late as twenty-five years after the menopause. As no studies of the ovaries were made, his assumption of persisting ovarian function in such cases is not justified; and we believe this very improbable, on the basis of our own histologic studies.

The few studies which have been made on the physiologic status of the senile ovary are inconclusive and contradictory. It has generally been accepted, as W. Waldeyer stated sixty-five years ago (1870), that complete atrophy of the follicular structures occurs within a few years of the menopause. In the case of experimental animals physiologists have been able by hypophyseal implants to reestablish ovarian function; but there is much doubt whether in the human being such a result can be accomplished by any available method of administration of anterior pituitary or anterior pituitary-like gonadotrophic principles. Only Westman has reported the finding of corpora lutea in the ovaries of 2 postmenopausal women who had received injections of pregnancy blood, but his conclusions are not generally accepted by other workers (L. Waldeyer). Tschertok and Penkow report negative results in 7 cases in which somewhat similar studies were made, though in these, pregnancy urine was used for the preoperative injections.

It seems clear, nevertheless, that after the menopause, the functional activity of the ovary may persist for a time, especially so far as the production of estrin is concerned. This is comparable to the prepubertal development of follicles and production of estrin, followed later by anovulatory and still later by ovulatory cycles, which so often characterizes the inauguration of menstrual function at puberty. Just how long after the menopause this estrin-producing capacity may persist, however, is a problem which only future histologic and endocrinologic studies can settle.

COEXISTENCE OF HYPERPLASIA AND ADENOCARCINOMA

The most provocative aspect of our study, however, has emanated from the examination of 104 cases of actual adenocarcinoma, because in a surprisingly large proportion the uninvolved endometrium shows definite hyperplasia, while in other cases there is a history of menopausal bleeding strongly suggesting hyperplasia at that epoch, a suspicion which in 4 cases can be proved because the tissue from curettings done at that time has been available for study. Moreover, in 5 others there was a history of one or more curettements done elsewhere at about the menopausal age, presumably for functional bleeding, though the slides could not be secured. In 6 other patients there was a definite history of menopausal flooding, though no operation had been done at that time.

When we use the term "hyperplasia" in connection with this group of cases, it should be made plain that we do so in the very broad sense in which it has come to be employed, i.e., as indicating the picture which is considered to be due to excessive estrin stimulation. As already stated, the diagnosis of this condition in women of reproductive age is often colored by the clinical history of bleeding, while the chief histologic criterion available to us, aside from absence of secretory activity, is a varying degree of proliferative activity, whether it be an unusual development of the epithelium of the smaller glands, abundance of stroma, or cystic distention of some of the glands, with possibly a "Swiss-cheese" pattern. It is in this sense that we have used the term here, for the problem with which we are concerned is not so much the relation to cancer of full-blown hyperplasia as of those proliferative conditions which may be considered to be of estrogenic origin.

The typical mucosa of women well beyond the menopause is thin and atrophic, with fibrotic stroma, and with occasional and usually moderately dilated glands. This, at any rate, is the kind of endometrium we expect to find after ablation of the ovaries in either the human being or the lower animals. When an infection of such an endometrium occurs, as in senile endometritis, the cystic distention of glands is more pronounced, and the distended glands often contain cell-detritus or leucocytes, instead of being empty or containing the clear albuminoid transudate which is so common in either the normal or the hyperplastic endometrium. In fact, it would seem logical to believe that this transudate, if such it be, is evidence of increased hyperemia and possibly of excessive estrin stimulation, a view supported by the fact that when this albuminoid content is conspicuous in senile endometria, one can usually find other evidences of proliferative activity, such as a thickened proliferative type of gland epithelium in the smaller glands or a very active looking stroma. To put it another way, many of the various grades of so-called senile endometrium show evidence of a hang-over or persistence of estrin activity.

It is our impression that in the senile endometrium, as in that of the reproductive epoch, one can distinguish all grades of estrin effect. At one extreme is the very atrophic type in which the estrin effect is apparently in complete abeyance, at the other the genuine hyperplasia of hyperestrinism, with various intergrades between these two extremes. This observation checks up with the reports which are now being made in increasing numbers as to the finding of estrin in both the blood and the urine of elderly women. The term "senile endometrium," therefore, is a chronologic rather than a histologic one, for it does not refer to any one characteristic histologic picture. Paradoxical as it may seem, it will embrace even some cases of hyperplasia.

It need not be emphasized that difficulties of histologic evaluation are at times encountered, especially if numerous cystic glands are observed, so that a "Swiss-cheese" gland pattern may be simulated in an endometrium which is not hyperplastic. Even in the hyperplasia of reproductive life, it is quite common to find flattening of the epithelium of the larger cystic glands, while on the other hand, one may see very active epithelium in some of the cystic glands of the senile endometrium. In either the senile or the hyperplastic endometrium, the gland lumina are either empty or they contain an eosin-staining albuminoid fluid, the significance of which no one knows, but which is quite certainly not a retention product, for it is often found in endometria which show no gland distention whatsoever.

When, therefore, evidence of such proliferative activity has been pronounced, we have included the cases in this group of hyperplasia coexisting with carcinoma, though in the great majority the endometrial pattern was of the "Swiss-cheese" type characterizing the frank variety of hyperplasia. In all such interpretations, as in the diagnosis of hyperplasia in cases of functional bleeding, we are faced with the difficulty of trying to interpret physiologic abnormality on the basis of histologic change, but we believe our criteria have been those commonly accepted.

Not only do adenocarcinoma and hyperplasia frequently coexist, but in many instances one can see in one and the same case, and perhaps in one and the same section, all grades of transition from frankly benign, to borderline, to obviously malignant histological pictures. Altogether we have studied 104 cases of corporeal adenocarcinoma, and in fully 25 of these (24.03 per cent), we have found a coexisting hyperplasia of the endometrium. The significance of this figure is increased when we bear in mind that in 40 of our cases, sections through noncancerous mucosa were not available for study. Of the 64 cases in which both cancerous and noncancerous mucosa were available for study, fully 39.06 per cent showed hyperplasia, an incidence which to us was most astonishing. In case after case we find pictures like those shown in Figs. 12, 13, 14, and 15, showing the two lesions side by side. In some, like Fig. 12, one can trace the transition by definite gradations from benign hyperplasia,

to a proliferative borderline stage, merging almost insensibly into out-and-out cancer. It is therefore in these cases of postmenopausal hyperplasia rather than in those far more commonly seen in the reproductive epoch that some sort of relationship to cancer seems clearly established.



Fig. 12.—Benign hyperplasia on the left, passing on to markedly proliferative pattern on the right, beyond which (though not shown in the picture) was a definite adenocarcinoma.



Fig. 13.—(Gyn. Path. No. 39555.) Typical benign hyperplasia below, adjoining equally typical adenocarcinoma above. Patient aged fifty-nine years.

It is of interest to compare the incidence of hyperplasia in normal women well beyond the menopause with hyperplasia in the women with adenocarcinoma in the same age group. The age of fifty-five years was arbitrarily selected as the basis for this comparison. Of 804 cases of hyperplasia with accurate data as to the age, 40 occurred in women

beyond fifty-five, an incidence of 4.8 per cent. On the other hand, 61 of our 104 adenocarcinoma patients were beyond fifty-five, and 13 of these showed an associated hyperplasia, an incidence of 21.3 per cent. It is probable that this figure would be much higher were noneancerous endometrium available for study in all of our cases. In 40 of our cases, as already stated, there was no such tissue for study. Even when it was, it was usually only the endometrium immediately adjoining the cancer area.

The suggestion arising from the above comparison would be that there must be some relationship between this disproportionally high incidence of hyperplasia in the cancer cases and the development of cancer. What this relationship is no one can say in the present state of our knowledge,



Fig. 14.

Fig. 14.—(Gyn. Path. No. 36910.) Coexisting hyperplasia (at bottom) and adenocarcinoma, in patient of fifty-nine years.

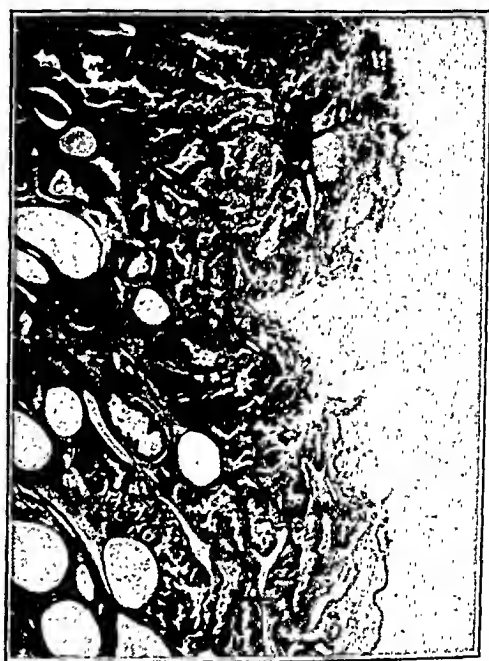


Fig. 15.

Fig. 15.—(Gyn. Path. No. 38689.) Below and to left is seen a typical hyperplasia pattern, while above and to the right is seen adenocarcinoma. Patient aged sixty-two years.

though various possibilities can be thought of. Does a hyperplasia persisting after the menopause predispose to the development of cancer? This would seem to be the case, and, since the only known cause of hyperplasia is a persisting hyperestrinism, the natural assumption would be that it is this factor of abnormally long-continued subjection of the endometrium to estrin stimulation which is the important predisposing influence. Crossen and Hobbs have recently reported a statistical study of the menopausal ages of women with adenocarcinoma, indicating a high incidence of late menopause in such cases. It seems likely that hyperplasia and its causative hyperestrinism must have been factors in the delayed menopause.

We feel quite conservative in using the term, "predisposing," as regards the relation of hyperplasia to adenocarcinoma, for there are many who now look upon estrogenic substances as actually carcinogenic. The studies of Lacassagne, Overholser and Allen, Hofbauer, Cori, and others, all revolve about this concept. We shall not review the evidence along this line, for this constitutes a story in itself; but a few especially pertinent observations may be noted. Lacassagne was able to produce mammary cancer by theelin injections in male rats of a species in which the males are relatively immune to spontaneous mammary cancer. On the other hand, Cori's experiments have shown that the very early castration of mice, of a strain with notoriously high cancer incidence, confers immunity to cancer. Large amounts of estrin have been found in the blood of both male and female cancer patients (Dingemans, Freud, de Jongh and Laqueur), while the follicle-stimulating principle of the anterior hypophysis has been found in the urine of 81.8 per cent of women suffering with various forms of genital cancer (Zondek). Schön has not only confirmed the finding of estrin in women with genital cancer, but she has found that the hormone disappears from the urine after complete removal of the cancer, to reappear again if recurrence of the tumor takes place. At times, however, estrin is not found with even extensive cancer.

This question is fascinatingly bound up with the newer investigations as to the chemistry of the sex hormones, and as to the close chemical kinship of the latter with certain well-known nonhormonal substances which are known to be carcinogenic as well as estrogenic. To this group belong certain sterol derivatives, tar, the bile-acids, and certain vitamins. Some of this newer work has been discussed in a recent paper by Novak; it has been much more fully reviewed in a recent publication by Leo Loeb. The latter states, as regards the above-mentioned experiments with mammary cancer, that "it may be regarded as established that estrogenic substances, as a rule acting in association with hereditary factors, may be strongly carcinogenic; but such carcinogenic action is restricted to the tissues of the mammary gland with which they combine and in which, under normal conditions, they induce growth processes."

Especially pertinent to our present problem is the fact, as emphasized by Loeb, that the cancer produced by estrogenic substances, as well as that produced by the tar hydrocarbons, is preceded by a preparatory stage, beyond which cancer follows even though the carcinogenic factor ceases to operate. The changes produced are gradual. In the case of the tar hydrocarbons, and presumably also with the estrogenic hormones, there is a capacity "to induce the transformation of normal into cancer tissues at any point in which they come into long-continued contact with tissues, whether they are of epithelial or of connective tissue origin, provided they still possess the potentiality to grow and proliferate."

Here, then, on the basis of sound experimental work, we apparently have an explanation, not only of the carcinogenic possibilities of the hyperestrinism which underlies the occurrence of hyperplasia, but also of the frequency with which one encounters gradations of proliferative activity which represent, as it were, stepping-stones to cancer. It thus seems not inappropriate, in so far as the endometrium is concerned, to speak of actual transitions to cancer, a phrase ordinarily shunned by general pathologists, and perhaps quite properly so as regards cancer in general.

Another hypothesis which suggests itself in explanation of the frequent finding of hyperplasia in cancer long after the menopause is that perhaps the carcinoma itself acts as the estrogenic factor and is thus responsible for the production of the hyperplasia pattern in the endometrium. This explanation seems less tenable than the one already discussed, chiefly because of the not rare finding of hyperplasia in postmenopausal women who do not have cancer. While certain carcinogenic substances are also estrogenic, there is no evidence that cancer itself is. It is possible that both the hyperplasia and the carcinoma may be due to an increased or perverted function of some endocrine organ, whether this be the pituitary or some other gland, which is responsible for the production of estrin in old women; though this explanation is also entirely hypothetical. An abundance of experimental work, some of which has already been quoted, indicates that prolonged and excessive estrin stimulation may predispose to or induce cancer, so that this order of events, rather than the reverse, would seem likely as regards the relation of hyperplasia and cancer. Finally, although there is no direct evidence on this point, one must at least think of the possibility that an estrogenic effect in old women may be of chemical rather than purely hormonal nature, possibly as a result of some metabolic change involving the sterol substances which have been shown to be estrogenic.

SUMMARY

The evidence presented in this paper points to a relationship of some sort between hyperplasia of the endometrium and corporeal adenocarcinoma. The material studied includes 804 cases of hyperplasia and 104 of adenocarcinoma, encountered in a review of 12,813 cases passing through our laboratory during an eleven-year period (Jan. 1, 1925, to Jan. 1, 1936). While in the overwhelming majority of cases hyperplasia is a very frankly benign lesion, a small minority (14 of our 804) reveals evidences of marked proliferative tendencies which may even simulate cancer.

The histologic characteristics of benign hyperplasia present degrees and variations which are discussed in the paper, as are the proliferative and pseudomalignant pictures at times encountered (stratification, adenomatous proliferation, marked atypicalness of glands, syncytium-

like epithelial proliferation, squamous metaplasia of gland or surface epithelium, etc.). Atypical gland proliferations, simulating adenocarcinoma, are especially frequent in the polyps so often seen with hyperplasia.

An interesting finding in this study was that hyperplasia is not rare in women long after the menopause (40 of 804 cases); and the etiology and significance of this are discussed. The occasional occurrence of hyperplasia with bleeding in elderly women lessens the significance of these findings as pointing to the probability of granulosa-cell carcinoma of the ovary, unless an ovarian tumor can actually be palpated.

In the study of the 104 cases of adenocarcinoma, the most impressive result was the demonstration of a coexisting hyperplasia and adenocarcinoma in fully 25 of the cases in which some of the noncancerous endometrium was available for study. Since the great majority of the adenocarcinoma cases (78 of 92 in which we have accurate age data) were beyond the menopausal age, this at once suggests that a postmenopausal hyperplasia, or, perhaps more accurately, the endocrine dysfunction responsible for it, must strongly predispose to the development of adenocarcinoma. Since a persistence and relative excess of estrin is accepted as the cause of hyperplasia, it would seem that it is this endocrine factor which must be suspected as the one predisposing to cancer genesis.

It should be emphasized that the ordinary hyperplasia of the reproductive epoch is not only frankly benign from the histologic standpoint, but also that it has no apparent predisposing influence in the causation of adenocarcinoma during menstrual life. It would seem from our studies that it is the postmenopausal persistence of hyperplasia which is in some way bound up with the occurrence of the common postmenopausal type of adenocarcinoma.

The question of the relation between estrogenic and carcinogenic substances, and the carcinogenic properties of estrogenic substances, is discussed in our paper. Whether the persisting estrin stimulation in cases of postmenopausal hyperplasia serves merely to keep up a form of chronic irritation, or whether its carcinogenic effects are more direct and fundamental, cannot be answered as yet, though the latter seems, in the light of recent experimental work, to be the more likely explanation. In our own cases of coexisting hyperplasia and adenocarcinoma, we have in some been able to show a definite transition of the benign to a borderline and then to an undoubtedly malignant pattern: so that, in the endometrium at least, it would seem that we are dealing with histologic intergrades between benign and malignant lesions. When such pictures are encountered in the endometrium obtained by diagnostic curettage, there is often a justification for the dictum, "Nicht Karzinom, aber besser herans."

Since, on the basis of these observations, hyperplasia is to be classed as a preneoplastic lesion, in the sense of one predisposing to later adenocarcinoma, it would at first thought seem that we should all the more generally recommend abolition of ovarian function by x-ray or radium in the treatment of functional bleeding of the menopause. Whether or not this would be of any practical value, however, is questionable since it seems quite certain that other sources of estrogenic substance than the ovary must be reckoned with.

One must be struck with the analogy of this problem to that of the breast, in which likewise the ovarian hormones can produce either very benign forms of cystic mastitis, or more markedly proliferative pictures which are scarcely or not at all distinguishable from cancer. In still another field, the cervix, we are now finding similarly puzzling borderline pictures, though we know almost nothing about their possible endocrine relationships. We refer particularly to leucoplakia and, even more, to the intraepithelial carcinoma or Bowen's disease, in which the epithelial layer presents all the characteristics of cancer except for invasiveness, and which are quite similar in appearance to the growing margin of an actual cancer. Are such lesions in themselves benign, as would seem to be indicated by the fact that they have often been cured by the most conservative procedures? Or are they inevitable precursors or very early stages of cancer, which, as in Bowen's disease of the skin, may not develop invasiveness and other malignant characteristics until the lapse of perhaps many years? Finally, may such lesions represent the response of the cervical epithelium to abnormal endocrine stimulation?

In all three of these fields, cervix uteri, corpus uteri, and breasts, we have to deal with the possible rôle of ovarian hormones. This seems significant in view of the growing opinion that the carcinogenic possibilities of estrogenic substances are most to be reckoned with in those organs in whose growth and activities estrin normally plays an important part.

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DISCUSSION

DR. RICHARD W. TELINDE, BALTIMORE, MD.—For several years there have been references to this subject in the literature, but the conclusions arrived at by the several authors vary markedly. Cullen, the first gynecologist to describe hyperplasia, concluded that it bore no relation to malignancy. In Burch's most recent paper he says, "I have never seen the two conditions together in the same patient nor have I seen hyperplasia as a forerunner to cancer." Fluhmann and Stephenson in a review of 22 cases of adenocarcinoma found no traces of hyperplasia associated with it. In 1923 Robert Meyer reported 4 cases of early carcinoma occurring in hyperplastic endometrium. He cautions his audience not to assume that this is a common occurrence for, to quote him, "These few cases . . . have come to light only after long years of collecting and investigating." In contrast to the conclusions reached by these men, Howard Taylor in 1932 presented evidence from which he concluded that "when the hyperplasia is at all marked, the possibility of a predisposition to the development of cancer should be considered and the case regarded with the same degree of suspicion now bestowed upon the diffuse form of hyperplasia of the breast epithelium." He presented two cases of carcinoma of the endometrium from his laboratory in which previous curettings had been diagnosed hyperplasia. But, he frankly states that on reexamination it was found that carcinoma had been overlooked in the original curettings.

And now Novak and Yui find the astonishing incidence of nearly 40 per cent of hyperplasia in the 64 cases in which both cancerous and noncancerous mucosa was available for study. How can we correlate these findings with those of Fluhmann, Burch and Meyer? It would seem that the most likely explanation is a difference in their interpretation of what constitutes the minimum histologic changes necessary to a diagnosis of hyperplasia. There are no absolute criteria for the diagnosis. I have had the opportunity of examining the material upon which Novak and Yui made this study, and, frankly, their histologic interpretation of hyperplasia is more liberal than mine.

In order to give myself a background for the study of these slides I first studied several nonmalignant postmenopausal endometria. A certain number of cystic glands are frequently encountered and the fact that they are almost invariably filled with a clear secretion and that the epithelium is almost always greatly thinned suggests to me that they are retention cysts. But there are some postmenopausal endometria in which the histologic picture is remarkably like that of premenopausal hyperplasia, but in my judgment they are relatively rare. Dr. Novak has shown that 4.8 per cent of his 504 cases of hyperplasia occurred after fifty-five years, but he did not give us what percentage of postmenopausal benign endometria showed this histologic pattern. In studying 20 postmenopausal endometria picked at random from our laboratory I found the same histologic picture which Novak and Yui have

interpreted as hyperplasia in 11 cases. This is an incidence of 55 per cent as compared with an incidence of 40 per cent in their carcinoma cases. This causes me to question its etiologic significance in the carcinoma group.

If hyperplasia is a precancerous lesion one would expect a parallelism between the age incidence of hyperplasia and carcinoma. The greatest incidence of hyperplasia is in the fifth decade of life. After fifty the incidence of hyperplasia decreases but the incidence of adenocarcinoma increases, so instead of a parallelism in their incidence there is a divergence. I have assured innumerable women in the late forties or early fifties who have had recurring bleeding due to hyperplasia that after getting past the menopause their chance of further trouble due to the hyperplasia would be nil. I have never had one of these women return with carcinoma of the endometrium. But even if an occasional one is later a victim of carcinoma, is it more than one might expect on the law of chance?

If we are to change our concept of hyperplasia from a purely benign lesion to a precancerous one, the next logical step is to modify our present conservative treatment in a radical direction. This I feel would be a mistake, and it is with the thought of preventing unnecessary radical surgery or radiation that I have brought up these objections to the acceptance of an attractive theory which does not coincide with my clinical or pathologic experience.

DR. FRED J. TAUSSIG, St. Louis, Mo.—We are at present engaged in an analysis of corpus cancer cases at our hospital and have found that of the patients operated upon, the average age was fifty-five. In general we were not impressed with the frequent occurrence of a late menopause. We were, however, struck with one peculiar thing, that there were 5 patients on whom a diagnostic curettement had been done with a microscopic report of hyperplasia. Vaginal hysterectomy was performed in spite of the negative findings and carcinoma was found in the uterus on removal. There were only three patients in our series in whom there was a definite history of a preexisting hyperplasia.

I have been particularly interested in the relationship between hyperplasia and adenocarcinoma in young individuals, since I have had two very striking instances suggesting a connection. In one patient, aged fifteen years, a curettement was done and a polyp was removed with resulting six months' amenorrhea. Then at the age of nineteen years with a return of the menorrhagia, curettement was again done and the sections were diagnosed as hyperplasia, but Dr. Otto Schwarz made this comment, "This case bears watching." Within a period of one year the bleeding returned and a large polypoid mass was found protruding at the external os about the size of a thumb. Biopsy showed definite and well-developed adenocarcinoma of the body of the uterus. The patient refused hysterectomy and she was given 3,675 mg. hours of radiation. Upon my insistence she returned four months later and curettement at that time showed no more cancer. Four years have now elapsed, and there has been no recurrence.

The other patient was brought to me at the age of thirteen because of prolonged and excessive bleeding, which yielded promptly to corpus luteum extract hypodermically. At the age of seventeen there was a recurrence and the same treatment was employed with success. Two years after this, at the age of nineteen, she returned with the same symptoms and all therapeutic measures failed. She also refused removal of the uterus and x-ray treatment served only to check the bleeding for two months, when it returned more profusely than ever. Finally curettement was done and the particles removed showed early adenocarcinoma. A supravaginal hysterectomy was done over five years ago, and there has been no recurrence.

DR. C. FREDERIC FLUHMAN, SAN FRANCISCO, CALIF.—Studies made possible by freely obtaining biopsy specimens of the endometrium, as well as blood estrin determinations, have shown that the problem of hyperplasia of the endometrium is not

a simple one and that we may distinguish two conditions which yield a common histologic picture in the endometrium but which differ greatly in their clinical manifestation and functional behavior.

In the first place, there is the condition of an active "hyperplasia endometrii," or the "metropathia hemorrhagica" of Schroeder. Histologically, the endometrium presents the appearance so well described by Novak of a dense stroma, large proliferating glands, cystic glands, large blood vessels, and with many mitotic figures denoting marked growth activity. Clinically, these patients have enlarged, softened uteri and are characterized by cyclic or irregular uterine bleeding. And finally, the blood estrin tests, as I pointed out last night, show *not* a constant high content of estrogenic substance, a "hyperestrinism," but a definite increase which is associated with the onset of the hemorrhage. In the intervals between the periods of bleeding the blood-estrin may give normal values or negative reactions. This type of hyperplasia I have never seen in patients in the postlimacteric period except accompanying certain tumors of the ovary.

On the other hand, biopsy specimens of the endometrium have shown that a histologic picture essentially indistinguishable from "hyperplasia endometrii" may occur under very different conditions. I have found it, for instance, in 12 patients with longer or shorter periods of amenorrhea. These women may show small atrophic uteri. They do not bleed, and blood-estrin tests give normal values or negative reactions. The condition may persist for months or years as repeated biopsies have shown. These patients may very well be said to have a "hyperplasia endometrii," but they do not present the same condition as those of the first group. The endometrium does not show the same intense growth activity, nor the presence of many mitotic figures. It is, so to speak, a "passive form," and although it can be demonstrated in the postlimacteric, in my experience it is comparatively rare. If this should be the condition that Novak refers to, it is indeed remarkable that this type, the so-called passive form, should be associated with malignancy, whereas in early life the active form with its intense cellular activity should be a relatively benign state.

And, finally, although the concentration of estrin in blood and urine rises during the postmenopausal period, it is in association with involutional changes in the uterus and vagina. If it were possible for it to stimulate a growth activity of the endometrium one would certainly anticipate abnormal uterine hemorrhages preceding the actual development of the carcinoma.

As Dr. Stephenson and I pointed out in a previous communication, a study of the material available in the Stanford Gynecological Laboratory does not suggest any relationship between hyperplasia and carcinoma except the possibility of their co-existence. It seems to me that one must accept with hesitation any theory which would make us regard hyperplasia endometrii as a "precancerous" condition.

DR. NOVAK (closing).—In the group of cases which I presented, of adenocarcinoma together with hyperplasia in the adjacent mucosa, I am frank to say that the matter of differentiation from senile endometrium did not at first occur to me, because the histologic picture seemed so different from that of the latter. After going over some of the sections with Dr. TeLinde, I added several paragraphs to our paper to emphasize why, in our opinion, these pictures could not be mistaken for simple senile endometria. In our own informal discussion, Dr. TeLinde laid great stress upon the fact that some of the glands show a flat epithelium and some show a pale-staining liquid or albuminoid exudate. Neither one of these objections seems to me valid.

In the perfectly typical hyperplasia of reproductive life, it is very common to find flattening of the epithelium in many of the cystic glands, while an albuminoid exudate is often seen not only in typical hyperplasia but also in the normal endome-

trium. Certainly it cannot be interpreted as a retention product, and I do not know of anyone who has so considered it. To illustrate these points, I am throwing on the screen a number of slides from Schröder's monograph, all showing typical hyperplasia, but showing also flattening of the epithelium of some of the large glands and also the albuminoid exudate under discussion. I am showing also, from the same author, a typical hyperplasia from a woman many years after the menopause.

Both of the discussants seem to me to have missed the chief point of the paper, since both speak of the lack of parallelism between the age incidence of hyperplasia and of adenocarcinoma. We tried to make it plain that the hyperplasia of menstruating life seems to have no relation with cancer, but that if the postmenopausal endometrium is subjected to persistent estrin stimulation, there is apparently a real predisposition to cancer. A chronic irritation may be of little importance in a young person, but may predispose to cancer in the older patient. And the same thing may be true of a persistent hormonal irritation.

Dr. Fluhmann speaks of two different varieties of hyperplasia, but we have not been able to make any such distinction in our laboratory. He suggests that the kind of hyperplasia we have found in these older patients is like that which one finds in amenorrhea. This seems strange, since it is rather generally accepted that these cases of "polyhormonal" amenorrhea in which hyperplasia is characteristically found are due to an excess of estrin stimulation.

To produce cancer there must admittedly be some unknown constitutional predisposition or dyscrasia, together with some local factor, most often chronic irritation. We believe that our work indicates that postmenopausal proliferative activity of the endometrium, due to an estrogenic stimulation of as yet unknown source, constitutes such a local predisposing factor, and that it is related to the development of a considerable fraction of our cases of adenocarcinoma of the corpus uteri.

Fauvet: *The Genesis of Brenner Tumors*, Arch. f. Gynäk. 159: 585, 1935.

Fauvet describes four cases of Brenner tumors of the ovaries in detail. He does not believe that these tumors are comparable to endometrioses because they are always ovarian in origin while the endometrioses are not necessarily so. He is inclined to agree with Schiller that the Brenner tumor arises from the ovarian rete rather than with Walther's cell focus theory. He believes that they arise as a result of hypoovarianism rather than from hyperfunction of the ovary. An analogy is made with Behring's statement regarding hemorrhagic metropathy, chronic cystic mastopathy and endometriosis, namely that these are "paramenstruations" and result from dysfunction rather than from hyperfunction of the ovaries. He believes further, that there exists a connection between these tumors and the adrenals although he is unable to prove this.

RALPH A. REIS.

Chi, Li, and Yang: *The Presence of Carotin in Ovarian Tumors*, Chinese M. J. 49: 751, 1935.

The authors describe a case of dermoid cyst of the ovary, combined with pseudomucinous cystadenoma, which had spontaneously ruptured and resulted in extensive peritoneal implantations. This condition is generally known as pseudomyxoma peritonei. The fluid contents of such tumors may be colorless or brownish; the latter color is probably due to the presence of altered blood pigment. In the author's case carotin pigment was present in large quantities. The patient also had a high content of carotin in the blood.

C. O. MALAND.

SECONDARY SEQUELAE AFTER INTERPOSITION OF THE UTERUS

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(From the Department of Gynecology, New York Post-Graduate Medical School and Hospital, Columbia University)

BETWEEN the years 1914 and 1918, in a special clinic for cystoscopy of the female, some forty patients with bladder complaints, who had been subjected to interposition operations by others, came under observation. At that time the indications for the operation were not clearly defined and the technic had not been perfected. Occasional instances of unsatisfactory results encountered thereafter, as well as the recollection of the first group of cases, discouraged the use of this operation for several years, until a careful consideration of the technical details convinced me that the undesirable sequelae could be eliminated. Mackenrodt, Dührssen, Watkins, Wertheim, Schauta, and others have contributed to the present-day technic, which probably varies somewhat in different clinics. For the past ten years I have done the operation in selected cases of procidentia and large cystocele with considerable satisfaction and without the embarrassment of subsequent therapeutic problems. This has been due to restricting its application absolutely to women past the menopause, as well as to a proper regard for certain precautions which suggested themselves, as the causes of unpleasant end-results were analyzed. The purpose of this discussion is to crystallize the causative factors of surgical disappointments rather than to submit statistics on personal operative successes, which will be reviewed in a subsequent communication.

CYSTITIS

Immediate postoperative cystitis is but little more frequent after interposition of the uterus than after other pelvic operations which necessitate manipulations of the bladder. It can be minimized by the avoidance of trauma, intravesical instillations of protargol after each postoperative catheterization, and the routine use of hexamethylenamine. On the other hand, a number of patients complain of the onset of bladder annoyances long after their discharge from the hospital, and are found to be suffering from chronic trigonitis. Usually several months elapse before the urinary frequency and dysuria appear and the patient seeks relief. Cystoscopic examination discloses an elevation and marked congestion of the vesical trigonum, with small additional depressions on either side, suggesting that the operator neglected to mobilize the bladder sufficiently laterally before pulling the uterus forward

(Fig. 1). This eventuates in putting the trigonum on the stretch on the posterior surface of the anteverted uterus and initiates a local circulatory stasis. The delay in the manifestation of the symptoms may be due to the fact that bacterial infection does not occur early. Culture of the urine after the patient presents herself usually reveals colon bacilli, although the *Staphylococcus aureus* is sometimes the offender. I have found the most useful therapeutic agents in the treatment of the patient's symptoms to be 7.5 gr. doses each of hexa-



Fig. 1.—The operator has pushed the bladder well off the cervix in the mid-line, but has neglected to mobilize it laterally, before opening the uterovesical peritoneal fold.

methylenamin and sodium benzoate every four hours, with intravesical instillations of a 20 per cent solution of oil of cajeput in sterile olive oil three times a week. Several weeks usually elapse before the patient is comfortable without treatment. Preoperative and postoperative cystoscopic examinations are always desirable. Delayed cystitis can be avoided in most instances if the bladder is freely mobilized laterally during the dissection which detaches it from the cervix.

VESICAL CALCULI

Three patients have presented themselves complaining of marked diurnal and nocturnal frequency, severe tenesmus, and agonizing suprapubic discomfort. One had calculi in each of two lateral depressions,

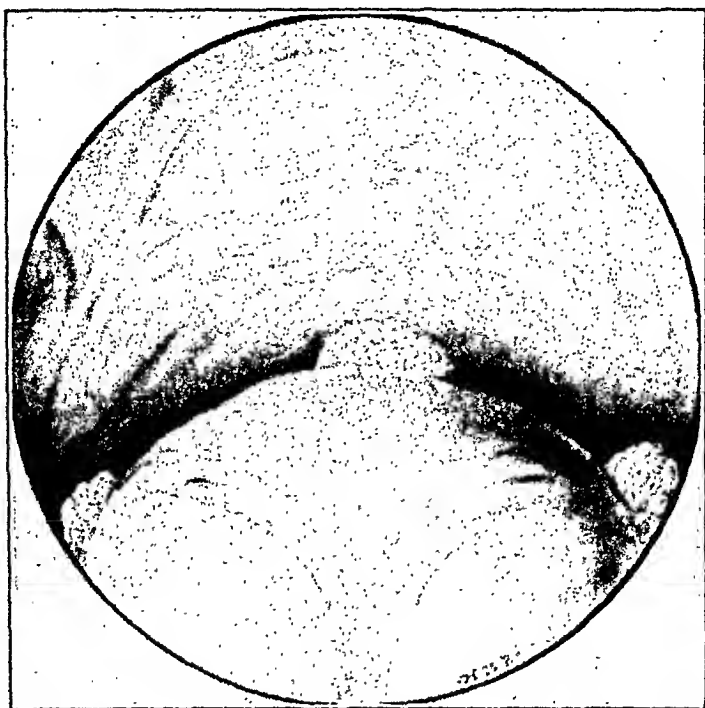


Fig. 2.—Calculi in each lateral depression and the posterior pocket.

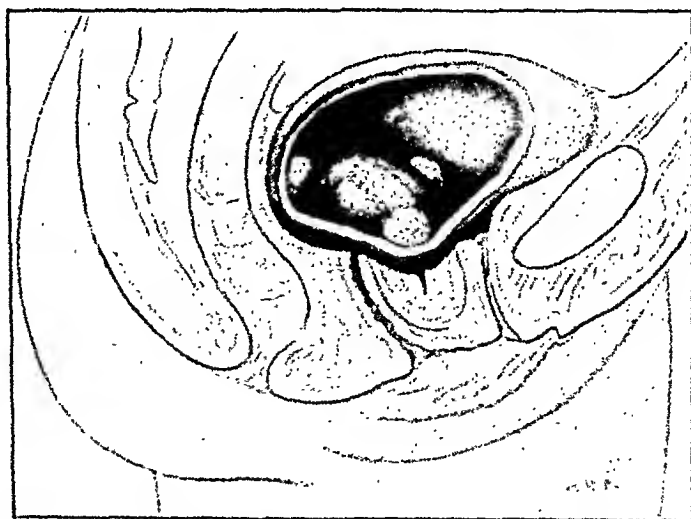


Fig. 3.—Lateral aspect of the bladder floor stretched over the underlying uterus (bladder greatly distended).

another had a stone in a large posterior pocket in the bladder behind the underlying corpus, and the third had multiple concretions in both lateral and posterior areas (Fig. 2). The urine was extremely turbid and loaded with colon bacilli in all three cases. The operations had been performed from six to 18 months before these women came under

observation. Evidently the operators had not only failed to mobilize the bladder sufficiently laterally, but two of them had also sutured the cut edge of the uterovesical fold of peritoneum too far back on the posterior surface of the cervicocorporeal junction. The latter error fixes the floor of the bladder at a level below that of the trigonum, thereby creating a posterior pocket which tends to harbor residual urine (Fig. 3). The urinary stagnation, plus the incidental passive congestion resulting from the stretching of the bladder floor, invite early bacterial infection, crystallization, and calculus formation. When the cut peritoneal margin is sutured to the surface of the posterior aspect of the extremely anteposed uterus, it should be stitched only so far back as it can be without causing tension on the bladder floor.

URINARY INCONTINENCE

Incontinence may be a symptom before operation and cured by it; or the lack of control may persist after the interposition. The relief of this preoperative disturbance can be almost assured by preceding the major steps of the operation with a Kelly plication of the vesical sphincter, although the freeing of scar tissue in the region of the urethro-cervical junction and the interposition alone may suffice in an occasional case of uterine prolapse without much cystocele. It is wise to introduce two infolding mattress sutures at the bladder neck in all cases in which incontinence is a symptom. I have seen one neurotic patient who complained of a gradual loss of control several years after an interposition operation. In this instance, the annoyance may have been just another expression of the underlying neurosis.

PREGNANCY

In 1919 a multiparous patient in the childbearing age was subjected to an interposition operation by a surgeon who carefully sterilized her by tubal resection. Three months later I was confronted with a uterus nearly four months pregnant. The only way in which this paradoxical situation could be explained was that a curettage had not been done before the interposition and the impregnation had antedated the operation. Anticipating a possible rupture of the uterus before term due to an asymmetrical development and distortion of the corpus, I made the mistake of evacuating the uterus with a placenta forceps and curette through the cervical canal. Although the therapeutic abortion was accomplished, it was a difficult procedure. In two other cases of pregnancy in a transposed uterus, the gestation sac and decidua were easily removed by vaginal hysterotomy, after splitting the anterior vaginal wall (Fig. 4). I have not had the fortitude to assume the responsibility for carrying a patient to term after an interposition operation, and believe that menstrual life is a distinct contraindication for its selection. However, many gynecologists do utilize the operation in women who have not reached the climacterium, and rely with confidence upon tubal resection to prevent pregnancy. Under such circumstances the

endometrial cavity should always be curetted prior to the interposition to remove a possible attached fertilized ovum. Carl H. Ill¹ reported two cases of full-term pregnancy in young multiparas after the interposition operation with careful tubal sterilization by double ligation with linen thread, canterization, and burial of the stumps. The first patient was in labor four days and was delivered with forceps; the second had a classical cesarean section. In the discussion of Ill's paper at the meeting of the New York Obstetrical Society, a number of similar cases were described, with complications presenting various difficulties. Hurd confessed to having omitted a curettage on one occasion, delivering the



Fig. 4.—Vaginal hysterotomy, illustrating case of evacuation of early gestation sac.

patient at term nine months later. Watson stated that he regarded interposition of the uterus as a "bad operation." A series of therapeutic problems following interposition, such as those presented during the discussion of Ill's paper, should help to establish menstrual life as an absolute contraindication. Pregnancy is a highly undesirable sequel; first, because labor is likely to be complicated, and second, because the dynamics of parturition may undo the operation.

RECURRENCE OR PROLAPSE

Several cases of "recurrence" have come under observation, one as early as ten months and another as late as seven years after operation. There are three varieties of postoperative vaginal protrusion. First,

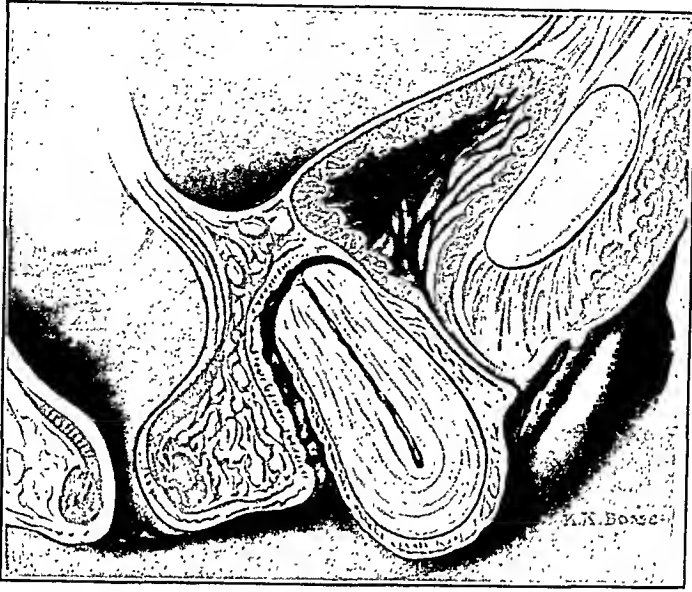


Fig. 5.—Reverse prolapse of the uterine corpus due to failure to suture the cornu to the subpubic structures.

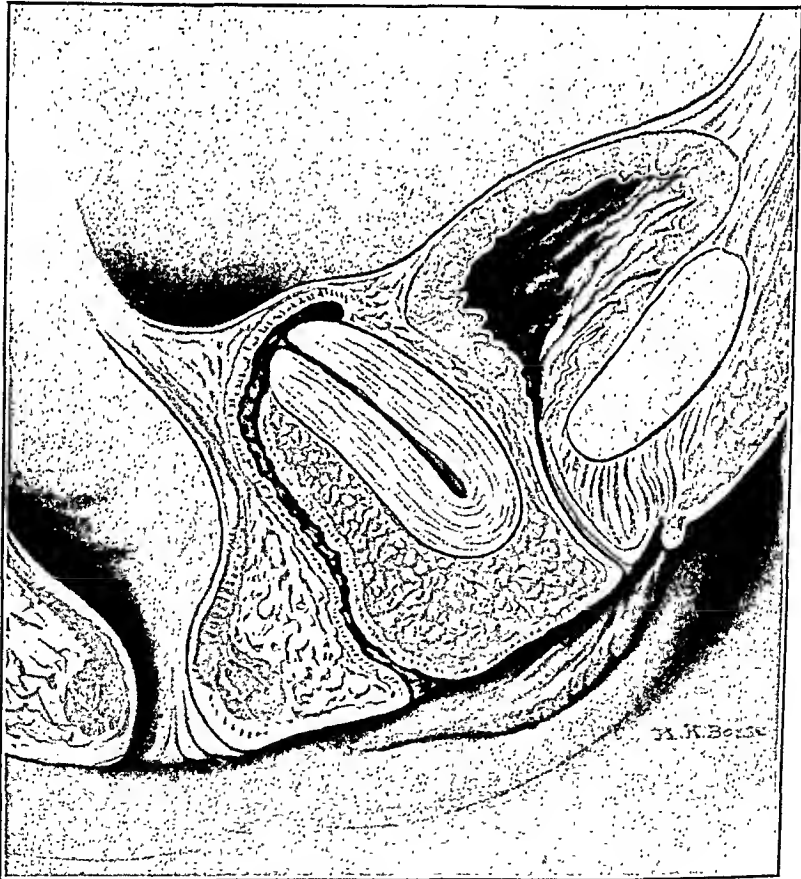


Fig. 6.—Redundancy of anterior vaginal wall, causing vaginal bulging, due to insufficient trimming of mucous membrane flaps.

that in which there is more of a reverse prolapse with bulging of the vaginal wall covering the overlying fundus than a return of a procidentia. The descent of the corpus is exaggerated when the patient strains, and it seems to be trying to dive "head-first" out of the vagina (Fig. 5). This can be ascribed to the fact that, although the uterus and vaginal wall flaps were correctly coapted and sutured, the fundus was not firmly fixed by stitching the cornu on each side to the periosteum

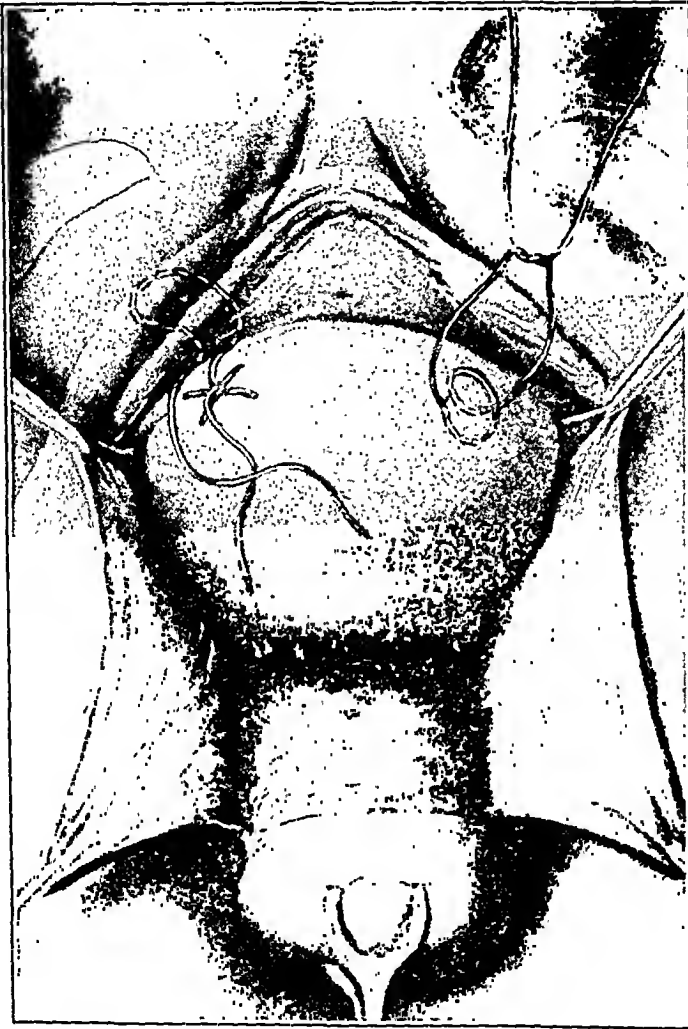


FIG. 7.—Fixation sutures of Pagenstecher linen, placed in the cornu on each side, and sutured to the firm tissues under the pubic arch.

under the pubic arch. Second, that in which there is really a recurrence of the prolapse, the uterus breaking away from the vaginal wall as a result of defective suturing or neglect to shorten the uterosacral ligaments when a high rectocele is present. And third, an apparent post-operative bulging of the vaginal mucosa when insufficient tissue has been resected laterally in trimming the flaps (Fig. 6). All of these defects are a source of discomfort to the patient, and create the impression of an operative failure.

In reoperating on these women, it is surprisingly easy to mobilize the structures concerned in the original procedure and re-do the operation. All of these embarrassing end-results can be avoided by (1) suturing the uterine cornu on each side to the subpubic periosteum with Pagenstecher linen (Fig. 7); (2) placing four interrupted master chromic sutures on the surface of the uterus, being careful to insert the lowest exactly at the junction of the corpus and cervix, as advocated by Phaneuf,² to obliterate the angle at the isthmus and throw the cervix

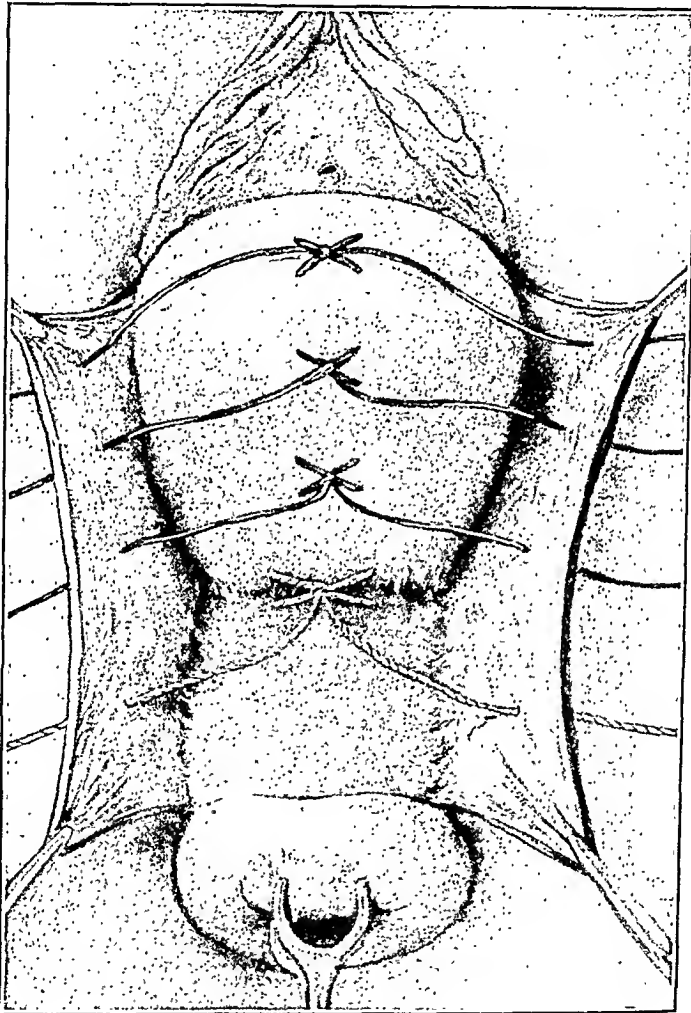


Fig. 8.—The lowest of the four master interrupted sutures (accentuated in the illustration) should be placed exactly at the cervicocorporeal junction, as advocated by Phaneuf, to obliterate the angle at the isthmus. (This step is shown before amputation of the cervix.)

well back (Fig. 8); (3) exact trimming and approximation of the vaginal flaps over the uterine corpus, without tension on the one hand, or redundancy on the other; and (4) adequate plastic repair of the perineum and posterior vaginal wall with high fixation of the rectum. When the uterus is so extremely atrophied that it is inadequate to support the heavier bladder, the Mayo vaginal hysterectomy is obviously better insurance against recurrence than interposition of the uterus.

One of the most common causes of postoperative vaginal bulging is the neglect of a posterior vaginal hernia. When an enterocele is associated with a prolapse, it must be corrected simultaneously, by free mobilization of the sac, reduction of its contents, resection, and high fixation.

FIBROMYOMA

Three patients who had been subjected to interposition operations sought relief from severe menorrhagia due to fibromyomatous tumors, two, five, and eight years, respectively, after operation. One patient was thirty-nine and the other two were forty-four years of age. In the first, the tumor was a soft myoma as large as a two months' pregnancy, and responded satisfactorily to 1,500 mg. hours of radium therapy. In the second, there were multiple hard nodules and the uterus was immobilized. They were removed by abdominal hysterectomy, which was difficult to perform without jeopardizing the bladder and ureters. In the other, the multilobular tumor mass was as large as a six months' pregnancy. Hysterectomy was regarded as unduly hazardous, radium therapy was contraindicated and would probably have proved useless, and roentgen ray therapy was employed. Hemorrhage was arrested, but the patient still suffers from a sensation of weight in the pelvis and urinary frequency. Cystoscopy shows marked extravesical pressure. It is possible that the tumors were present in each of these patients at the time of the operation and were overlooked by the surgeon. Nevertheless, such cases are a further argument against the use of the interposition operation in women who have not reached the menopause. The development of new fibroid tumors is certainly uncommon after menstruation ceases, whereas the activation and enlargement of small intramural nodules is not unusual at any time before then. When fibroids are present, or suspected because of a large uterus, or there is profuse or irregular bleeding, hysterectomy is always preferable to interposition.

CARCINOMA

One case of carcinoma of the corpus was subjected to a panhysterectomy without any particular technical difficulties. An early fundal carcinoma coexistent with the prolapse can be excluded or detected by a preliminary curettage. No instance of carcinoma of the cervix has been encountered, probably because the cervix is customarily amputated at the time of the interposition. A bleeding prolapsed uterus after the menopause should invariably be removed.

CONCLUSIONS

1. Interposition of the uterine will cure ptosis of the pelvic viscera in carefully selected cases.
2. Delayed sequelae, recurrence of prolapse, and untoward end-results can be prevented by proper attention to technical details.

3. The interposition operation should be discarded as an elective procedure in all women before the menopause.

4. The bladder should be manipulated with the utmost gentleness during the operation, but must be freely mobilized laterally.

5. Lateral and posterior pockets in the bladder floor predispose to calculus formation. The uterovesical peritoneal edge should not be sutured too far back on the posterior surface of the anteverted uterus.

6. A Kelly plication of the urethrovvesical junction should be done on all patients who complain of urinary incontinence.

7. If the interposition operation is performed during menstrual life, the patient should be sterilized by tubal resection. All patients should be curetted to remove an existing fertilized ovum or to detect an early fundal carcinoma.

8. Recurrence of prolapse can be prevented by suturing the uterine cornu on each side to the subpubic structures, straightening out the angulation at the cervicocorporeal isthmus, accurate trimming of the vaginal flaps, and adequate plastic repair of perineal lacerations, rectoceles, and posterior vaginal hernias. Recurrence can be corrected by re-doing the operation.

9. A subsequent fibromyoma or carcinoma of the uterus is more likely to develop in a uterus transposed before the menopause than after it.

10. A postmenopausal bleeding uterus should be removed rather than transposed.

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580 PARK AVENUE

DISCUSSION

DR. JOSEPH L. BAER, CHICAGO, ILL.—A few years ago I reported to this Society a series of 220 patients with prolapse, treated by 11 different operative procedures. Among those procedures the interposition operation held the leading place, being used in 40 per cent, or 91 patients. For a great many years the gynecologic staff at the Michael Reese Hospital had favored this operation, hence the dominant position that it held. At the beginning of 1929 we began to interest ourselves in other methods of procedure, and the interposition operation has now a frequency of something less than 10 per cent instead of 40 per cent.

I am in accord with each of the points made by the essayist with perhaps the exception of the contraindication to the use of the interposition operation in women during menstrual life. Operative sterilization was done in 49 of our series and there was one postoperative x-ray sterilization. We had just one subsequent pregnancy. That patient was allowed to go to term and at term was treated by a section and sterilization. I am not as much afraid of a subsequent pregnancy as is the essayist because one of two things happens: either the patient aborts spontaneously, or the uterus is emptied by the operator in early pregnancy or at term.

Our immediate postoperative results in that series of 90 were as follows: 1 death occurred from embolism; 38 patients had a temperature of 101° for one or more

days; 10 had 101° or more for seven days. The complications included an infected perineum in two instances, an infection of the perineal wall which persisted for several days, pelvic abscess in two instances, and sepsis and shock in one patient with satisfactory cure.

In connection with treatment of the bladder, the man who originally devised this operation emphasized freeing the lateral attachments, as described by Dr. Dannreuther. Failure to do so has resulted in "horseshoe bladder" and not infrequently there has been calculus formation. Spalding advocated dividing the ligaments on each side in order to meet specifically that problem in the operation. Catheterization was not required in over one-half of our series, 57 per cent. There was very little postoperative cystitis.

The hospital stay averaged seventeen days. In follow-up examinations there was a satisfactory result in 92 per cent of those whom we were able to reach, which is a very high percentage of satisfaction with this operation. The important preoperative symptoms had been protrusion, backache, and urinary frequency.

I do not favor Pagenstecher linen for fixing the cornua to the periosteum, but prefer kangaroo or forty-day chronic catgut. It is important that the fundus be anchored just back of and under the symphysis, for if it is in front of the symphysis or merely under it the fundus may protrude. It is vital that the cervix be amputated if the uterus is more than 8 cm. in length.

In replacing the interposition operation in these last eight years, we have added two others to our repertoire. One is the vesicofixation operation of Halban-Porges, which is excellent but not so good for the large cystocele type but which gives excellent fixation and has the advantages of the interposition operation. The second is the modified Fothergill with which we are becoming more and more pleased as the years go by. I think it may some day take first place for cure of prolapse of the uterus. Neither of these operations requires sterilization.

DR. RICHARD W. TELINDE, BALTIMORE, MD.—There is a procedure employed in the Johns Hopkins Clinic postoperatively which I do not believe is in very general use. Some years ago one of our men when visiting Dr. John Clark's clinic found that they gave a liter of fluid by bowel while the patient was still in the operating room. I believe they used 5 per cent sodium bicarbonate solution with two or three ounces of mineral oil in the liter. This procedure assures a good quantity of fluid during the first postoperative hours.

We combine this with an instillation of 1 per cent mereurochrome into the bladder, not for any bactericidal effect, but because of its irritative properties. The bladder irritation gives rise to a desire to void as soon as the patient awakens from her anesthetic, and she often calls for the bed pan before she is fully conscious. She starts to void small amounts, 25, 50, 100 c.c., and within six or eight hours she is usually voiding 200 c.c. or more. We carry out this procedure as a routine in major gynecologic operations, including the interposition operation. Craig reported a series from our clinic some years ago and the incidence of one or more postoperative catheterizations was reduced 60 per cent to 7.7 per cent. If the output is 200 c.c. or more very few of the patients will be found to have residual urine.

IMMEDIATE REPAIR OF CERVICAL INJURIES

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(From the Department of Obstetrics and Gynecology of Northwestern University Medical School and of the Evanston Hospital)

MANY obstetricians and obstetric authors have taken a very conservative position concerning cervical injuries. Their attitude has been that routine inspection of the cervix is not advisable and immediate repair of cervical injuries should only be done when necessary for the control of bleeding. Some years ago I published the results of a series of cases in which immediate repair had been done, and since that time, we have continued to inspect the cervix after labor and to repair it at once if it appeared necessary. That the conservative stand of former years is beginning to be replaced by a more active one is evidenced by the appearance of papers by DeLee, E. P. Davis, Skeel, Bubis, Emge and, more recently, Goff and George Gray Ward. Goodall, in his monograph on puerperal infection published in 1932, expresses himself quite clearly when he says "it is my firm conviction that within five years it will be considered as bad practice in hospitals to leave a cervical tear unrepaired as it would be considered culpable today to leave a perineal tear unsewn."

There have been two arguments against immediate suture: first, that sutures put in while the cervix was soft and succulent, as it is immediately after labor, would not hold, and second, that infection might follow. An experience extending over a considerable number of years has convinced us that, with careful technic, satisfactory results are obtained in about three-fourths of the cases. We are also quite convinced that the fear of infection is greater than it need be. We have not been able to note any increase of morbidity which could be traced to cervical suture.

The importance of cervical lesions is sufficiently great that it appears warranted to inquire what may be done to decrease their extent. A very large part of cervical abnormalities are in whole or in part a result of the trauma of parturition. This is, in considerable part, unavoidable. The cervix of every woman who delivers a child is injured to some degree. In many cases the injury is so slight that a return to the condition which existed prior to labor is almost attained. In others the stretching or partial laceration of the tissues of the side of the cervix produces more or less ectropion after involution is complete. With the purpose of determining the character of labor which is most prone to produce injury to the cervix and the forms of interference which are most often followed by cervical damage, I have made a study of the

cervical injuries which have occurred in a series of cases in our service, noting the relationship of cervical injury to parity and to various forms of operative intervention. Routine examinations are made rectally, vaginal examinations being used only when the information obtained by rectal examination is insufficient. Chemical sterilization of the vagina is not employed.

I have gone over the delivery records of 3,534 patients, in which study I wish to acknowledge the assistance of Dr. R. M. Grier, in order to ascertain the type of labor in which lacerations of the cervix are most frequent. We also desired to ascertain the forms of delivery most likely to cause cervical injury. We have for a number of years made very liberal use of the outlet forceps operation. It has not seemed to us that this procedure could cause cervical trauma, as, at the time the forceps delivery is done, the head has already escaped from the cervix. Other operative procedures are far more likely to injure the cervix.

This series of cases contains 1,596 primiparas and 1,938 multiparas. It has been our custom for years to examine the cervix in all primiparas and in all multiparas, except those who have had a very easy spontaneous delivery. In all others the cervix has been exposed with specula and its entire circumference carefully inspected. All tears greater than 3 cm. in length are sutured. Small lacerations are let alone. After involution has taken place there usually appears only a small indentation, and in some cases the injury is no longer noticeable. In some cervices, in which notable lesions occurred during labor, a later ectropion may be found.

TABLE I

Total number 3,534	
Primiparas	1,596—11.2%
Multiparas	1,938— 4.1%
Both	— 6.3%

The routine inspection of the cervix consumes but little time and the additional manipulation has not increased morbidity. Adequate exposure must be obtained by a broad retractor upon the perineum. A narrower lateral retractor is, in most cases, also needed. The necessary exposure of the cervix should be done with light ring forceps of the type suggested by DeLee. Volsella should not be employed as they add to the wounds already caused by the labor and are likely to tear the soft, succulent cervix. Goff has drawn attention to an important point in the visualization of cervical injuries. If the ring forceps grasps the anterior and posterior lips at the middle point, the softness of the puerperal cervix permits it to stretch and to be drawn out to such a degree that a laceration at one side is difficult to recognize. The ring forceps should grasp the cervix at points roughly corresponding to 2 and 4 and 8 and 10 on the clock dial. Only gentle traction must be used, merely enough to steady the cervix and hold it in position for inspection and suture. I have included in this series only those lacerations which seemed to re-

quire attention, that is, those of 3 cm. or more in length. Small injuries heal well. It is often stated that large ones do. If this is so, the origin of the deep lateral defects found in many cervixes is difficult to explain. In primiparas injuries of this extent were found in 11.2 per cent, in multiparas in 4.1 per cent, an average for the entire series of 6.3 per cent.

If primiparas are considered alone, we find a definite variation in the incidence of injury in the cases of anterior vertex presentation as compared with posterior vertex or breech. These figures are shown in Table II.

TABLE II. PRIMIPARAS

L.O.A.	711	63 tears— 8.8%
O.D.A.	403	29 tears— 7.2%
O.D.P.	254	41 tears—16.1%
L.O.P.	166	34 tears— 8.0%
Breech	63	12 tears—19.0%
Others	7	1 tear — 6.0%

The number of right anterior positions in this report seems to me to be too great. This is probably due to the fact that some cases were recorded by the interne as anterior which were posterior earlier in labor. Dilatation is slower in posterior positions, and the operative interference often needed to terminate the labor may influence the number of lacerations. Cervical lacerations in breech deliveries in primiparas are notably increased, there being injury which required surgical attention according to the standard given above in 19 per cent.

TABLE III. MULTIPARAS

L.O.A.	969	42 tears—4.3%
O.D.A.	551	24 tears—4.3%
O.D.P.	197	11 tears—5.5%
O.L.P.	130	9 tears—6.9%
Breech	79	1 tear —1.2%
Others	6	0 tears—0

In multiparas the difference in frequency in anterior and posterior positions is much less marked, but the frequency of injury is somewhat greater in the posterior position. In Table IV, in which primiparas and multiparas are assembled, a marked difference in incidence of injury appears, the number being definitely greater in posterior occiput and in breech positions.

TABLE IV. PRIMIPARAS AND MULTIPARAS

L.O.A.	1,680	105 tears— 6.9%
O.D.A.	954	53 tears— 6.5%
O.D.P.	451	52 tears—11.0%
L.O.P.	296	43 tears—11.1%
Breech	142	13 tears— 9.1%
Others	13	1 tear — 7.6%

Spontaneous delivery occurred in 1,470 patients, of which 264 were primiparas. Of the primiparas 36, or 13.6 per cent, sustained lacerations.

tions which needed attention. In the multiparous deliveries, 1,206 in number, only 4.1 per cent received injury. It seems worthy of emphasis that notable cervical injury may occur a little less often than once in seven cases.

TABLE V. SPONTANEOUS DELIVERY

Primiparas	264	36 tears—13.6%
Multiparas	1,206	50 tears—4.1%
Both	1,470	86 tears—5.1%

In the primiparas delivered operatively, there is a widely varying incidence of injury as is shown in Table VI. It is interesting to note that

TABLE VI. TYPES OF OPERATIVE DELIVERY. PRIMIPARAS

Low forceps	1,090	105 tears—9.6%
Midforceps	77	22 tears—28.6%
High forceps	1	0 tears—0.0%
Version—forceps on after-coming head	13	3 tears—23.3%
Version—no forceps	9	2 tears—22.2%
Breech extraction with forceps	28	8 tears—28.5%
Breech extraction—no forceps	33	3 tears—9.0%

in the cases terminated by outlet forceps delivery, laceration was found in 9.6 per cent, while the primiparas who delivered normally had tears in 11.2 per cent. I believe that the explanation for this difference lies in the fact that, as we are accustomed to use outlet forceps very freely, only those primiparas deliver spontaneously who are progressing rapidly. The frequent use of forceps, especially in primiparas, when the head is upon the perineum, if skillfully done, is a conservative rather than a radical procedure. Injury to the cervix in these cases occurs nearly always, if not invariably, during the last third of the process of dilatation. We have many times found injured cervices in cases in which the last part of the first stage had progressed rapidly, when we were quite certain that no laceration existed earlier. The incidence of injury was not influenced by the forceps operation. We have observed that in primiparas, whose cervices dilated rapidly, lacerations were found after delivery in a number of cases. It seems that a very rapid first labor is not invariably an unmixed blessing. A thickened edematous cervix may increase the difficulty with which lacerations are seen. This condition is found in women whose labors have been long. Cases of posterior position in which the anterior lip has been traumatized between the head and the symphysis may produce this condition. Submucous hemorrhage is seen resembling the color about a black eye. After a normal labor the cervix is not greatly thickened.

Experience in a number of clinics appears to indicate that outlet forceps deliveries skillfully done do not subject either the mother or the child to increased risk. The cervix participates in this immunity to increased injury. This would seem inevitable, as, when an outlet de-

livery is done, the head has already escaped from the cervix. In multiparas the incidence of injury is less than 1 per cent greater in outlet forceps deliveries than in spontaneous births. Midforceps, however, shows a great increase in cervical injury, 28.6 per cent in primiparas

TABLE VII. TYPES OF OPERATIVE DELIVERY. MULTIPARAS

Low forceps	532	26 tears— 4.8%
Midforceps	26	3 tears—11.5%
High forceps	1	0 tears— 0.0%
Version plus forceps	18	1 tear — 5.5%
Version—no forceps	20	0 tears— 0.0%
Breech extraction—plus forceps	19	1 tear — 5.2%
Breech extraction—no forceps	44	0 tears— 0.0%

and 11.5 per cent in multiparas. Many of these cervixes dilated slowly, and among them are a considerable number of cases of posterior position which required some form of interference. Midforceps deliveries are not done until it appears that complete descent will not take place or, at least, will not occur within a safe length of time. An active second stage is not permitted to continue more than two hours unless definite progress is being made. An unduly prolonged second stage exposes the woman to the possible danger of a retraction ring. In comparing the number of tears in primiparas delivered by version and extraction and those in whom the breech position was present primarily, we find that breech extraction without preceding version and with forceps on the after-coming head shows a higher incidence of injury than version and extraction or extraction without forceps. All patients with breech presentations are delivered, if possible, by the Mauriceau maneuver, forceps being used if any difficulty is encountered and if more than a very moderate force is needed. This causes the forceps to be employed chiefly in the cases in which the head does not easily slip through the cervix. In these cases the Piper forceps are very useful. Intervention before dilatation is complete in breech presentation is a serious error.

A consideration of the results of this series indicates that properly done outlet forceps deliveries do not increase the incidence of cervical injury. The number of injuries which require surgical attention according to the standard already given is probably greater than many obstetricians believe.

For the management of cervical lacerations various plans have been proposed. It has seemed to us that immediate repair is preferable to

TABLE VIII. TYPES OF OPERATIVE DELIVERY. PRIMIPARAS AND MULTIPARAS

Low forceps	1,622	131 tears— 8.0%
Midforceps	103	25 tears—24.2%
High forceps	1	0 tears— 0.0
Version—plus forceps	31	4 tears—12.9%
Version—no forceps	29	2 tears— 6.8%
Breech extraction—plus forceps	47	9 tears—19.1%
Breech extraction—no forceps	77	3 tears— 3.9%

suture done later during the puerperium, on the fifth or the tenth day. It is true that immediately after labor the cervix is soft, but due attention to technic is followed by results sufficiently satisfactory to make the plan worth while. It is true that in some instances a notch in the cervix may indicate the location of the tear at the end of the puerperium. If the major portion of a deep injury may be made to heal, the resulting ectropion is reduced or prevented.

In order to obtain healing which is satisfactory a rather definite plan must be followed, the essential points of which will be indicated. DeLee, some years ago, pointed out, and we have confirmed his observation by the examination of many lacerated cervixes, that the muscular structure of the injured cervix retracts, so that the cross-section of the torn edge of the cervix forms a "V," the two arms of the "V" being the mucosa of the cervical canal and the vaginal surface of the cervix, respectively. The sutures then must go sufficiently deep to grasp the retracted muscle. If the suture passes only through the arms of the "V," or the edges of the mucosa, it will inevitably cut through. The operator must sacrifice to a certain extent the desire to make an extremely neat suture line and place the suture deeply enough to grasp the muscular portion of the cervix. As the tissues grasped by the suture are very soft, they must be tied with but little force. In the presence of an abundant blood supply, healing is rapid. Suture material of long life is, therefore, not needed. Care must be exercised during the placing of sutures that too much traction is not put upon the cervical lips in the desire to obtain good exposure. It is easy to stretch them or to elongate one more than the other, thus causing an uneven approximation.

It has been logically urged by a number of writers that an attempt should be made after labor to restore the cervix to as nearly normal a condition as possible. It seems even more reasonable that the obstetrician should endeavor to decrease the need for restoration. Primary cervical repair is a procedure for the hospital and for the obstetrician. The physician who is not trained in vaginal plastic work should pursue the older and more conservative course of suturing only those cervixes which bleed sufficiently that hemorrhage must be controlled.

Our experience would indicate that the employment of the more serious forms of interference should be as limited as possible. Outlet forceps delivery does not increase the incidence of cervical injury. Bags should be used as infrequently as possible and manual dilatation, or Dührssen's incisions should be employed only upon the clearest indication. In the management of the lacerations which occur in spite of this conservative treatment, primary repair appears definitely to lessen later cervical abnormality.

DISCUSSION

DR. EDWARD A. SCHUMANN, PHILADELPHIA, PA.—Dr. Danforth's paper admits of little discussion because of the accuracy and soundness of his conclusions. I may therefore say with great brevity that lacerations occur with great frequency

even in vertex presentation; second, that we should not minimize the effect of the delivery of the shoulders in adding to the laceration of the cervix; third, that to our considerable surprise in the observation of a large number of patients treated by the so-called Slemmons' method of induction, our incidence of laceration was considerably reduced; fourth, that lacerations of the cervix, as of the perineum or of the anterior vaginal wall, are wounds requiring suture; fifth, that the discovery of cervical lacerations may in most instances be made with simple digital examination without exposure.

Last, repair of the cervix is productive of no increase in morbidity so far as our figures tell us, and is a procedure of great simplicity. The only point which we have found of value has been in a considerable number of cases of deep unilateral laceration to apply the lowermost suture first, carefully coapting the lips of the wound, climbing up the tear, as it were, rather than beginning at the apex.

DR. ROBERT L. DICKINSON, NEW YORK, N. Y.—I would like to say that this is one subject which we can perhaps best teach with pictures. Moreover, I speak for three-dimensional representations, and some day we are going to have adequate museums of models. My students were taught to repair, not on the living being, but by flexible molds of the severely lacerated pelvic floor and cervix. That is one of the ideas that I have never sold to the medical public but it is bound to come because you can only learn by doing. Having written two papers on this subject many years ago, I can speak with feeling. The first advocated immediate repair. The second reported the experiment of waiting for two or three days. There is an enormous edema and distortion immediately after delivery, the size of the anterior lip making it difficult to recognize the anatomy. This is also true of the pelvic floor injuries. Waiting until the edema had subsided, I could recognize anatomy that could not be recognized before.

DR. EARDLEY HOLLAND, LONDON, ENGLAND.—At home we are very conservative in this respect. Yet it seemed to me that, although the essayist had presented what I should call a radical measure, it was presented by a very conservative man.

Consideration of this matter leads at once to the question, of which is better domestic midwifery or hospital midwifery? There is not the slightest doubt that in a few years' time nearly every woman will have her baby in a properly equipped maternity hospital, and then we shall be able to do these things with impunity. But it would be dangerous to teach the students or the general practitioners that they should do prolonged repairs of the cervix, because if they did I am sure it would be disastrous. Yet I feel convinced that in our hospital work we should do repairs and that it will have a most astonishing effect in gynecologic practice. I suppose that the most common pathology we meet with in our practice is that of the cervix. When Dr. Danforth examines the patients in whom he has repaired the cervix, does he find what I would designate as a bell-shaped cervical canal? A very important point of technic must be the inclusion of all the retractor muscles in order to avoid finishing the repair later.

DR. DANFORTH (closing).—This operation is a specialist's procedure and not one which we teach to men who are going into general practice.

I believe I stated that we did not have 100 per cent perfect results. I do not think one can expect that, in dealing with a soft puerperal cervix, but the results are sufficiently good, so that we have been encouraged to continue.

One should be careful to get all of the muscular layers and this requires a suture which goes rather deeply. One must forego the desire to make an artistic suture line and place the sutures in what may appear to be rather a coarse manner. Plain catgut is preferable to chromic as healing is rapid.

RELATIONSHIP OF ACANTHOSIS NIGRICANS TO ABDOMINAL MALIGNANCY*

REPORT OF CASES, INCLUDING ONE IN WHICH THE PRIMARY GROWTH WAS IN THE PELVIS

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ACANTHOSIS NIGRICANS is a condition well recognized by dermatologists, and the microscopic picture of the cutaneous lesions is diagnostic. We are satisfied, however, that the condition and its significance are not well understood by clinicians and surgeons, especially as regards the adult types of the disease which are associated in the majority of cases with malignancy in the abdomen.

Acanthosis nigricans was first described by a dermatologist, Pollitzer, in 1890, and also independently in the same year by Janovsky. In 1909 Pollitzer reported a total of 53 cases in the literature, in 5 of which cancer of the uterus was present with extension to the sympathetic nervous system. Since attention has been called to the condition, many papers on the subject have been written, and about 250 cases have been reported. It is probable, however, that in many cases the condition is not diagnosed or at least is not reported. Pollitzer, in a discussion of Knowles's paper on the subject, said that 4 cases were not reported for every one that was.

Acanthosis nigricans may be divided into the juvenile and adult types. In the juvenile type, there are many supposed etiologic factors,^{2, 12} for example, those with a direct or indirect effect on the chromaffin and sympathetic systems, including metabolic disturbances; various toxins; achlorhydria; endocrine diseases, such as involvement of the thyroid gland, pituitary body, testes,⁴ ovaries, suprarenal glands, pancreas and thymus; inflammatory and traumatic conditions affecting the stomach and chromaffin system; congenital anomalies and hereditary factors, and tuberculosis. Even syphilis and the effect of sunlight on the enzymes in the skin have been incriminated. Actually the etiology of either the juvenile or adult forms of acanthosis nigricans remains to be proved. The juvenile type runs a benign course, except in rare instances such as in cases of perforation of a duodenal ulcer or in those of severe diabetes. There is no associated malignant condition.

We are especially interested in the adult types of acanthosis nigricans. The same factors that predispose to the juvenile form of the disease may occasionally be encountered in older people,¹ and the unexplained frequent association of acanthosis nigricans with cancer is of special concern.

*From the Mayo Clinic.

The cutaneous picture is the same in both the juvenile and adult types of *acanthosis nigricans*, no matter what the precipitating etiologic factor may be. The axillae, neck, external genitalia, and other flexural surfaces become pigmented, in that order. There are in addition to this pigmentation marked verrucous and papillomatous changes, hyperkeratosis and exaggeration of the normal cutaneous markings. In a third of the cases in which women are affected by the disease, the verrucous and papillomatous, and even condylomatous lesions, involve the labia and vagina. Lesions usually appear first in the axillae or on the neck, and in more than half the cases there are changes in the mucous membranes, although pigmentation is a much less frequent finding in the latter cases.

In the early stages of *acanthosis nigricans* very little thickening of the skin may be present, so that differentiation from Addison's disease may be difficult. While both Addison's disease and *acanthosis nigricans* show essentially the same distribution of pigmentation and both involve the suprarenal chromaffin and sympathetic systems either directly or indirectly, no explanation is available why in Addison's disease there is pigmentation only of the skin whereas in *acanthosis nigricans*, within a short period of time, there are in addition verrucous and other changes in the epidermis (Figs. 1 and 2). Hemochromatosis may be associated with increased melanin pigmentation, but again the accentuation of the markings of the skin and the verrucous changes seen in *acanthosis nigricans* are absent in the former condition. The latter changes are also lacking in other pigmentary dermatoses.

It is important to distinguish benign pigmentation with verrucous and papillomatous lesions which may be encountered in the axillae of women, and also extensive *verruca senilis* and *dermatosis papulosa nigra* in negroes from *acanthosis nigricans*.

The histopathologic picture is usually typical and, as has been said,⁸ is diagnostic. It is characterized by the following features: relative and absolute hyperkeratosis (increase in the thickness of the stratum corneum); marked irregular acanthosis (proliferation and increased thickness of the prickle cell layer) with adjacent areas of atrophy of the prickle cell layer; elongated narrow papillary bodies; dense melanin pigmentation of the basal cells of the epidermis; a few chromatophores laden with pigment, which are limited chiefly to the papillary bodies, and usually absence of any amount of inflammatory reaction in the cutis.

It is interesting to note that among patients with *acanthosis nigricans* who are less than twenty years of age malignancy is rarely, if ever, found, only one doubtful case of malignant deciduoma of the uterus, of a patient nineteen years of age, having been reported.¹³ Based on an analysis of Mukai's statistics for patients between twenty-one and thirty years of age, cancer may be associated with *acanthosis nigricans* in 23 per cent of cases, and for patients from thirty-one to forty years of



A.



B.

Fig. 1.—A, axilla; B, beneath breast: Showing increase in pigmentation, thickening of skin with accentuation of normal skin markings and warty lesions.

age in 53 per cent of cases. When patients are more than forty years of age, cancer is found in 75 to 80 per cent of the cases. The probability in such cases is that the primary tumor or a metastatic growth involves or presses on some part of the chromaffin or sympathetic nervous system and the outlook is always grave. In other cases liberated toxins are probably responsible.

The relationship between disease of the suprarenal glands and acanthosis nigricans is still debated by many authors, including Grace and Schwartz and Mook and Drews. Others do not believe that the disease, at least the adult type, is in any way related to disturbances of the endocrine system. On the other hand, the fact that the majority of cases reported (according to Mukai the total number of cases reported is 117 of juvenile and 94 of adult acanthosis nigricans and seven which he could not classify) are of the juvenile type and in them the disease develops during the active growing years, gives weight to the views expressed by some authors (Knowles and others) that the disease is of endocrine origin.

We have encountered 13 cases of acanthosis nigricans at the clinic, 5 of the juvenile type and 8 of the adult type. In 5 of the latter cases, the condition developed before the patients were forty years of age. In four cases acanthosis nigricans was shown by microscopic examination to be associated with abdominal malignancy (in three cases with cancer and in one with sarcoma). The following case (Case 1) is given in some detail because it illustrates the association of acanthosis nigricans with pelvic malignancy:

ACANTHOSIS NIGRICANS ASSOCIATED WITH PELVIC MALIGNANCY

CASE 1.—The patient, a woman, first came to the clinic in 1919 when she was forty-seven years of age. She had menorrhagia which was sufficiently severe to produce mild secondary anemia. She was given 410 mg. hours of radium treatment and was markedly benefited. She passed through the menopause about a year later with little trouble. She again returned to the clinic in 1926 with definite symptoms of exophthalmic goiter, and after appropriate medical treatment and partial thyroidectomy made an excellent recovery.

In 1928, or about eight years after her menopause, the patient again returned to the clinic complaining of irregular vaginal bleeding which was first noticed as a mere spotting shortly after thyroidectomy about two years previously. A diagnosis of degenerating hypertrophic endometrium was made from a curetted specimen. She was given 1,184 mg. hours of radium treatment and all bleeding stopped.

The patient was not seen again at the clinic until September, 1935, at which time she complained of an uncomfortable, dry feeling in her mouth, poor appetite, and the loss of twenty pounds (9.0 kg.) in four months. She had also noticed that since June, 1935, the skin of the axillae, of the neck, beneath the breasts, and in other regions was becoming darker and also verrucous. She had a history of qualitative food distress, with attacks of bloating and belching which, as a rule, were relieved by taking soda or by vomiting, but which on a few occasions had required a hypodermic injection of morphine. Jaundice was never noticed. She had no complaints referable to the pelvis but, on pelvic examination, an irregular fixed

mass could be felt which was larger than when she was last examined at the clinic seven years before. There had been no uterine bleeding in the meantime. A diagnosis of acanthosis nigricans was made (Figs. 1 and 2 *a*) with probable malignancy in the abdomen, and exploratory operation was advised.

After an interval of two months, the patient again returned complaining of cramping pains in the lower part of the abdomen and of increased loss of weight. Operation was again urged and the patient consented. Dec. 4, 1935, under general anesthesia, panhysterectomy was performed for an extensive adenocarcinoma of the body of the uterus, the growth being adherent to one loop of small bowel and to the base of the bladder and having extended out into the base of the left broad liga-

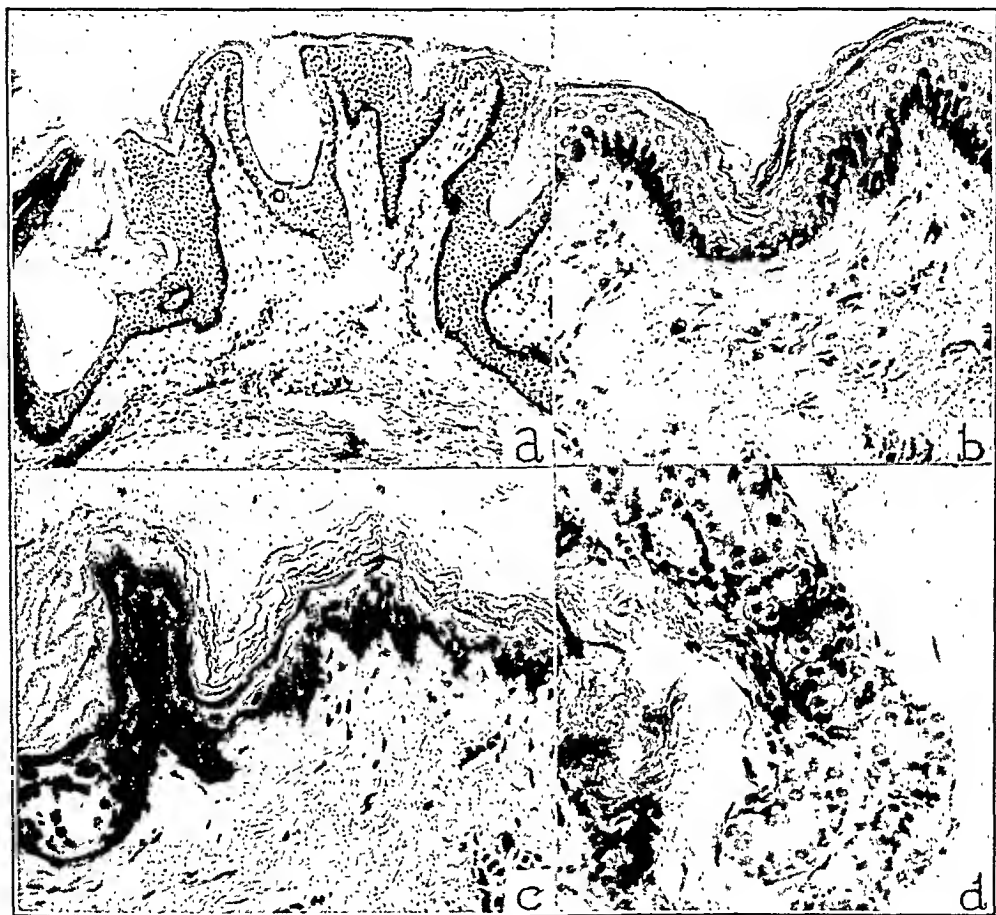


Fig. 2.—*a*, *Acanthosis nigricans* (typical picture); relative and absolute hyperkeratosis, keratotic plugging, irregular thickening of prickle-cell layer and increased pigmentation of basal cells of epidermis ($\times 80$); *b*, *Addison's disease*, typical capping of basal cells of epidermis with melanin and numerous chromatophores in the cutis laden with pigment; no significant changes in epidermis ($\times 320$); *c*, *Arsenic pigmentation*, relative and absolute hyperkeratosis, atrophy of prickle-cell layer, pyknosis and palisade arrangement of basal cells laden with melanin pigment; also, chromatophores in cutis ($\times 320$) (all silver nitrate and hematoxylin stains); and *d*, *hemochromatosis*, granules of hemosiderin of varying size (staining block) deposited in propria of sweat glands ($\times 320$ iron stain).

ment. The prospect for cure was not good because of the extent of involvement, but all visible evidences of the growth were removed. No apparent metastatic involvement of the aortic lymph nodes or liver was noted. Multiple gallstones were palpated in the gallbladder. One course of roentgen treatment was administered. This patient is, at the moment of writing (April 4, 1936) still alive and much improved; there is no indication of local recurrence or metastasis, although the pig-

mentation and verrucous changes have increased. There is a large plaque near the sacrum and involvement of the internal parts of the labia, as well as verrucous folds of the mucous membranes of the mouth but without pigmentation of the latter.

In the following seven cases of *acanthosis nigricans* of the adult type the condition was either definitely or presumably associated with abdominal malignancy:

ACANTHOSIS NIGRICANS ASSOCIATED WITH ABDOMINAL MALIGNANCY

CASE 2.—A man, thirty years of age, came to the clinic Dec. 28, 1921, complaining of indefinite pains in the upper portion of the abdomen and epigastrium. General physical examination gave entirely negative results, except for indicating marked pigmentation about the neck, axillae and inguinal folds, which the patient said had originated during the previous two months. He was dismissed. He returned about four months later after having continued to lose weight. The cutaneous lesions had become darker and there was definite thickening in these areas with warty-like growths. A clinical and histopathologic diagnosis of *acanthosis nigricans* with the possibility of malignancy in the abdomen was made. On April 14, 1922, the patient underwent an exploratory operation and multiple nodules were found in the liver. Microscopic study of these nodules revealed adenocarcinoma of Grade 1. The primary tumor could not be found. Convalescence was uneventful and the patient was dismissed April 20, 1922. We received information later that he died in August, 1922.

CASE 3.—A white man, thirty-eight years of age, came to the clinic Dec. 19, 1922, complaining of irritability of the stomach, which had been present for two years. In the fall of 1921 he had first noted the development of a brownish pigmentation on the first finger of his right hand. This had become more marked and later the skin of the entire body had become involved, pigmentation being more diffuse on all exposed areas and being particularly marked around sites of irritation, such as the waist band, calves of the legs and in the axillary and inguinal regions. The skin in these regions had become thickened and harsh. A diagnosis of *acanthosis nigricans* was made and confirmed histopathologically at the time of operation. At operation, December 23, an extensive carcinoma of the stomach was found and, because of obstruction, posterior gastroenterostomy was performed. The patient died about eight months later from carcinomatosis.

CASE 4.—A white woman, thirty-nine years of age, first came to the clinic July 14, 1925, because of obstruction of the common duct following cholecystectomy, which had been performed elsewhere. Gastroduodenostomy was performed because of gastric ulcer and the common duct was reconstructed over a catheter. Five years later she again returned to the clinic with jaundice. At this time there was also diffuse brownish pigmentation with thickening of the skin at points of pressure. Biopsy revealed the typical picture of *acanthosis nigricans*. The catheter was removed from the common duct and the patient recovered uneventfully. We learned that she died a year later, apparently from metastasis.

CASE 5.—A negro, fifty-six years of age, presented himself at the clinic Sept. 6, 1928, stating that about six months previously he had noted that the skin on his neck was becoming darker and that his hands were getting very rough. His tongue had become cracked and was thickened. The skin about his eyelids, in the axillae and groin, and about the joints had also become dark and thickened and he noticed generalized pruritus. There was a warty growth on his lower lip, and this was removed surgically. There were smaller warts on his lips, gum margins, and

face and hands. Beginning in January, 1927, he had been treated for ten weeks for gastric ulcer. The diagnosis of ulcer had been confirmed roentgenologically. Because of the close association of acanthosis nigricans (confirmed on this case by microscopic studies) and abdominal malignancy, exploration was thought advisable but the patient declined. He died Nov. 1, 1928, and postmortem examination was not made. The rapid onset of the condition and the fact that the patient died within a year and a half is strongly indicative of a malignant condition.

CASE 6.—A white man, twenty-nine years of age, came to the clinic July 16, 1929, complaining of itching in the axillary and inguinal regions of three months' duration. Verrucous lesions had then appeared and the skin had become very thick and dry. A general examination and detailed laboratory studies gave essentially negative results. A definite diagnosis of acanthosis nigricans was made. Exploratory operation was performed July 25, 1929, but with completely negative results. The patient died at home about five months after he was first seen at the clinic, the evidence on the basis of history, symptoms, and duration of the condition favoring a neoplastic process.

CASE 7.—A white woman, aged thirty-seven years, came to the clinic Feb. 22, 1932, complaining of rheumatism, dyspepsia, and menstrual irregularity. She had areas of deep pigmentation about the eyes, axillae, trunk, and genitalia. The left lobe of the liver was definitely palpable 10 cm. below the costal margin and examination of the fundus of the uterus revealed multiple uterine fibroids. The results of microscopic examination of a pigmented specimen of skin were strongly suggestive of acanthosis nigricans. On Feb. 13, 1936, we received the report of an operation which this patient had undergone. A supravaginal hysterectomy had been performed, with removal of the appendix. It was noted on exploration that the liver was enormously enlarged, and had a rounded edge and granular surface. The spleen was stated to be six or eight times normal size and the pancreas was enlarged and firm. An unusually large number of enlarged lymph nodes were said to have been present throughout the upper portion of the abdomen and along the great vessels of the back. Biopsy was not made at this time to rule out the possibility of malignancy. The patient's convalescence was uneventful.

CASE 8.—A white man, twenty-five years of age, presented himself at the clinic April 13, 1932, complaining of stomach trouble of five months' duration. At operation, March 1, an inoperable malignant growth was found in the stomach. Following extensive radium treatment there was marked improvement. On June 7, a second exploratory operation was performed and three-fifths of the stomach was removed. There was local lymphatic involvement and extension into the mesocolon. The pathologists reported lymphosarcoma. Convalescence was uneventful and further radium treatments were given. The pigmentation of acanthosis nigricans was then noted. The patient died on November 7, as the result of metastasis.

The following five cases are illustrative of acanthosis nigricans of the juvenile type:

ACANTHOSIS NIGRICANS OF JUVENILE TYPE

CASE 9.—An unmarried woman, aged twenty-four years, came to the clinic on Feb. 17, 1927. She was found to have a small centrally located adenoma of the thyroid gland which we did not think at that time was surgical. General examination was essentially negative. It was also found that her skin was darker than normal, and that this condition had been present approximately since birth. Her

skin had gradually become darker until she was twenty years of age, the condition having then become most marked around the mouth, neck, and abdomen. The skin then became thick and pigmented and verrucous lesions developed. A specimen of skin taken for biopsy confirmed the diagnosis of *acanthosis nigricans*. In a letter dated March, 1936, the patient stated that the cutaneous lesions and pigmentation had persisted.

CASE 10.—A married woman, aged twenty-three years, came to the clinic Sept. 2, 1929, complaining of stomach trouble. She was found at that time to have exophthalmic goiter and syphilis of the central nervous system. She also had hypertension and pyuria. Examination revealed marked *acanthosis nigricans* of both axillae, with a slight increase of pigmentation, which was confirmed histologically. There were also numerous pigmented areas on the body, with indurated and thickened skin, which the patient said had been present to some extent for eight and a half years. A specimen removed from the axilla for biopsy showed the typical picture of *acanthosis nigricans*. The patient had had fairly intensive treatment for syphilis before she came to the clinic, but this had no relation to, or effect on, the changes in the skin. She undoubtedly had a mild polyglandular dyscrasia; she had the male type of pelvis, trunk and extremities, irregular menstrual periods, and a tendency toward nymphomania. It is possible that some suprarenal deficiency played a part in the disease. A letter written in 1934 informed us that the patient had died on Jan. 10, 1932. She had had a stroke thirty days before her death. The local physician said she died of bacteriuria(?).

CASE 11.—A white woman, twenty-two years of age, came to the clinic Dec. 10, 1930, complaining of attacks of abdominal pain which occurred at indefinite intervals and began suddenly following dietary indiscretions. The pain was sharp and was localized in the right side. It was associated with nausea and vomiting and was usually relieved by soda, although on one occasion a hypodermic injection of morphine was necessary. General physical examination gave negative results. A roentgenogram of the gallbladder showed it to be functioning poorly and to be filled with stones. At operation, December 16, the gallbladder and appendix were removed because of subacute cholecystitis and chronic appendicitis. Convalescence was uneventful. The patient was then sent to the Section on Dermatology and Syphilology because of an acneiform eruption of the face. Early but definite lesions of *acanthosis nigricans* were found in the axillae. On subsequent examination, April 14, 1931, axillary lesions were found to be still present.

CASE 12.—A man of Norwegian parentage, aged nineteen years, presented himself at the clinic Feb. 27, 1931, for general examination. He offered no complaints except for persisting acne formation on his face, which had been present for about three years. Physical examination gave essentially negative results except for indicating excessive accentuation of pigment in the groin, axillary and flexural folds of the skin, and acneiform lesions on the face and back. A diagnosis of *acanthosis nigricans* was confirmed by biopsy. Roentgenologic examination revealed a duodenal ulcer with obstruction, and gastric analysis revealed a total acidity of 94, free hydrochloric acid of 82, and retention of 240 c.c. It was decided to defer exploration and have the patient return at monthly intervals for reexamination. He failed to return, however, until Feb. 20, 1935, at which time there was no change in the *acanthosis nigricans* and his general health was good.

CASE 13.—A married woman, aged twenty-nine years, was first seen at the clinic Nov. 13, 1934, because of pregnancy. Cesarean section was performed May 24, 1935, and a normal male child was delivered. The patient made a good recovery. She returned to the clinic on August 15 because of an infected mosquito bite on her ankle. She was found at that time to have hyperpigmentation in both axillae and

on the neck; she said that this had been present for ten years. A specimen was removed from the right axilla and the diagnosis of acanthosis nigricans was confirmed. There was no indication of any malignant condition at that time.

COMMENT

Our experience certainly indicates a definite relationship between the adult type of acanthosis nigricans and some abdominal malignant condition. In 10 of the 218 cases in the literature reviewed by Mukai the primary malignant growth was in the pelvis, in 7 of these cases being in the uterus. In one other case the growth was probably a Krukenberg tumor. Next to the stomach, the generative organs are the most frequent site of the primary malignancy in acanthosis nigricans. Metastatic lesions in the abdomen from cancer of the breast are not uncommon. Cause of death is known in 86 cases. In Mukai's article, which is the most comprehensive review of cases reported in the literature, the stomach was involved primarily in 58 cases (61 per cent) and the generative organs in 11 cases (11.7 per cent). Yet as Moncorps says, "The distinction between benign and malignant forms is not always a sharp one." However, most authors have failed to consider the relative percentage of malignancies according to decades of life.

The eutaneous manifestations in the adult type of acanthosis nigricans, according to some authors, may precede the systemic symptoms of malignancy by five to ten years; personally we would look upon the cases as having a juvenile type of acanthosis nigricans with the development in late life of malignancy; in other cases, eutaneous changes appear after a malignant condition is well established. In the majority of cases, however, the eutaneous changes and symptoms of malignancy develop about the same time. If there is any doubt about the diagnosis a specimen of skin should be taken for biopsy, and when the diagnosis is established, exploratory laparotomy is indicated in the case of adults, especially those in whom the onset is after forty years of age. When acanthosis nigricans develops after an operation for cancer, it usually signifies rapid cachexia and death. Involution of changes in the skin has been reported in only one case, and that was reported by Spietschka. In this case, that of a woman aged nineteen years, after a successful radical operation for probable uterine carcinoma the symptoms and signs of acanthosis nigricans entirely disappeared one and a half years later.

SUMMARY AND CONCLUSIONS

Acanthosis nigricans is probably attributable to a lesion or functional disturbance of the abdominal sympathetic system. When adults are affected, it frequently signifies an associated malignant condition in the abdomen. The probability is that the condition is much more common than published statistics would indicate.

Pigmentation is the result of a deposit of melanin in the basal or dendritic cells of the epidermis. It is symmetrical in distribution, being most marked in the axillae, on the neck, and around the genitalia and other flexural surfaces, including the umbilicus and under the breast. In this respect it resembles Addison's disease, but the verrucous and papillomatous changes permit differentiation both clinically and pathologically.

The prognosis in the juvenile type is good, whereas in the adult type it is grave, increasingly so in the later decades of life. Of the cases of acanthosis nigricans seen at the clinic, 5 of the juvenile type and 8 of the adult type, all the latter were probably associated with abdominal malignancy. Two of the 8 patients with the adult type of acanthosis nigricans are still living, 1, two months following operation elsewhere and the other five months following operation at the clinic. Next to the stomach, the uterus is the most frequent site of malignant disease in cases of the adult type of acanthosis nigricans.

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Item

American Board of Obstetrics and Gynecology

The next written examinations and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology will be held in the various cities in the United States and Canada on Saturday, November 7, 1936, and on Saturday, March 6, 1937.

The next general examination for all candidates (Groups A and B) will be held in Atlantic City, N. J., on June 8 and 9, 1937.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for these examinations must be filed in the Secretary's office not later than sixty days prior to the scheduled date of examination.

American Journal of Obstetrics and Gynecology

VOL. 32

NOVEMBER, 1936

No. 5

Original Communications

THE RÔLE OF THE LOWER UTERINE SOFT PARTS IN LABOR*

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INTRODUCTION

DURING the last three years at the Sloane Hospital for Women and the Roentgen Ray Department of Presbyterian Hospital, we have made extensive use of the roentgen ray in the study of fetal-pelvic relationships during labor. We have accumulated a comparatively large series of roentgenologic case studies, which, in many instances, consist of two or more sets of stereoroentgenograms for each patient, obtained at intervals during the first and second stages of labor. The method of delivery in the patients studied has varied from cesarean section after a trial of labor to a normal spontaneous delivery, so that we have had the opportunity of studying changing fetal-pelvic relationships in abnormal as well as in normal parturition.

The opportunity of comparing the fetal-pelvic relationship early in labor with the position which exists later, near the beginning of the second stage, has shown us the variable manner in which the fetal head may descend in relation to the pelvic cavity. Our observations have led us to attribute considerable significance to the lower uterine segment and its fascial attachments to the pelvic walls as the expla-

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

nation of these variations in the position of the pelvic axis of fetal descent. In the present report we wish to describe extreme examples of these variations, to explain the manner in which we believe the lower uterine segment and its supporting structures cause these diverse fetal-pelvic relationships, and, finally, to make brief reference to the resultant effect on the mechanism of labor in relation to the type of pelvis and the clinical course of labor.

METHODS

A complete roentgenologic examination during labor should include anteroposterior stereoroentgenograms obtained in the supine position and a large lateral film. The stereoroentgenograms and the lateral film should be compared to note any changes in the relationship of the fetal axis to the inlet or in the position of the head with respect to the pelvis which may occur unless the head is fixed in the pelvis. These differences between fetal pelvic relationships may be described as follows:

1. The anteroposterior roentgenogram may show that the fetal axis is markedly posterior to a perpendicular line from the inlet, while, in the same case, the lateral view may show that, as the uterus sags forward, the fetal axis becomes more perpendicular to the plane of the inlet.

2. The lateral film may also show that the fetal body and head have rotated slightly from the position which existed when the stereoroentgenograms were obtained.

3. Unless the head is fixed in the lower uterine segment it may be dislodged to a higher level in the pelvis when the lateral position is assumed. Or, in a few cases, it may actually descend to a lower level than the stereoscopic view revealed by virtue of the fact that the fetal body becomes more perpendicular to the inlet.

Anteroposterior stereoroentgenograms show undistorted spacial relations of head to pelvis and, for that reason, are superior to lateral views in the study of those variations in the fetal axis of descent which represent the chief objective of this present investigation. There are a number of reasons why the lateral views are not as satisfactory for this purpose. In the first place it is difficult to place the patient so that the anteroposterior diameter is parallel with the film. It is equally difficult to center the central ray at right angles to the anteroposterior diameter. Finally, the enlarged shadow image of the fetal head within the pelvic cavity, as seen in the lateral film, makes it difficult to appreciate its axis of descent in relation to the symphysis in front or the sacrum behind.

During labor the wet stereoroentgenograms may be viewed in the ordinary stereoscope and for practical purposes a true concept of the

spacial relationship of head to pelvis can be obtained. However, it is impossible to accurately control the size of the stereoscopic image of head and pelvis and we believe that some attempt to correct this undesirable physical fact is helpful. We have perfected a practical model of the precision stereoscope to serve this purpose. The wet films can be viewed immediately but, since the presence of developing frames makes it difficult to place the film correctly over the view box, some distortion of the image is inevitable, even in the precision stereoscope, though present to a lesser degree than would occur with the ordinary stereoscope. In a few cases the films, even when dried and viewed correctly in the precision stereoscope, may not be suitable for measurement, because the patient, through the discomfort of active labor, may move during the interval between the stereoscopic shift. However, under both circumstances, the precision stereoscope reconstructs a more accurate image with less distortion than occurs with the ordinary flexible stereoscope. These objections to the use of the ordinary stereoscope, for viewing either the wet or dried films, are not serious enough, however, to preclude its use when the observer is aware of the principles of stereoscopic distortion. The precision stereoscope makes it possible to see an exact reproduction of the pelvis and the fetal-pelvic adaptation. Any measurement desired may be taken. We are convinced that viewing the actual pelvis and seeing the fetal-pelvic adaptation are much more important than any linear or volumetric measurements.

OBSERVATIONS

(A) Normal Mechanism of the Lower Uterine Segment

In a recent publication¹ we discussed the general pattern of normal labor and made reference to the rôle of the lower uterine segment in molding and directing the head downward and backward into the pelvic cavity during engagement and descent. In view of the fact that at this time we concerned ourselves largely with variations in the position and degree of this downward and backward curved axis of descent, we must first briefly review the principles involved in the normal mechanism.

In normal labor the axis of the lower uterine segment causes the head normally to follow an axis in the posterior segment of the pelvis in relation to the sacral curve. This control exerted by the lower uterine segment and its supporting structures may be termed its "guiding" or "directing" influence. At the same time it causes flexion and molding of the fetal head. The degree of flexion or molding is, to a certain extent, dependent on whether the membranes are intact or ruptured.

Before the time of Robert Barnes² the function of the lower uterine soft parts was imperfectly understood. In 1869 he described the curved axis of descent referred to and attributed considerable significance to the inclined plane of the anterior wall of the lower uterine segment, believing that this plane deviated the head downward and backward into the hollow of the sacrum. He termed it the anterior or first "uterine valve." Barnes' views have received but scant recognition by modern obstetric authorities. We believe our observations have confirmed Barnes' principles, but the use of the roentgen ray has enabled us to study the effect which the factors outside of the lower uterine segment, especially the character of its fascial supports, may exert in modifying the position and degree of this curved axis of descent.

Further study of many x-ray examinations of normal and abnormal labor has convinced us that apparently the axis of the lower uterine segment does not always correspond to the optimum axis of the pelvic canal. In analyzing these cases we have arrived at the conclusion that the axis of the lower uterine segment must be influenced by its fascial attachments to the bony pelvis and that variations in this axis, caused by such attachments, exert a profound influence on the mechanism of labor.

The guiding influence of the lower uterine segment in normal labor and the principle of the variations in its axis, which concern us especially at this time, are illustrated in the case study shown in Fig. 1. The lower uterine segment has been outlined by the use of 6 per cent sterile sodium iodide solution held under pressure in the vagina at the time the roentgenograms were obtained. In the first roentgenogram obtained early in labor the head was situated over the fore-pelvis close to the symphysis, L. O. T. position, posterior parietal presenting and dipping well in the inlet. The sodium iodide was injected when the cervix was approximately three fingers dilated and well thinned out. This method of visualizing the lower uterine segment was used in a few cases without harm to the patient.

The axis of the outlined lower uterine segment in Fig. 1 (long curved arrow), through which the fetal head is descending, is slightly downward and backward and, as near as can be determined, represents the degree of curvature which occurs in normal labor. The fascial supports, which modify the degree and position of this axis, are situated between the vagina and the rounded portion of the lower uterine segment in the position indicated "X," Fig. 1. Note that the length of "A," which represents the distance between the posterior aspects of the symphysis and the anterior portion of the dilating utero-cervical junction, is greater than "B," the distance between the sacrum and the posterior aspect of the utero-cervical junction. Variations in

the length, strength, or character of these structures, "A" and "B," Fig. 1, will naturally affect the position of the axis of the lower uterine segment, thereby guiding the head downward in one extreme close to the sacrum, or in the other close to the symphysis.

It will be noted that these variations in the position of the axis of the lower uterine segment are attributed to the length, strength, and character of the fascial attachments, situated at a low level just above the cervix, "X," Fig. 1. At a higher level, as indicated in Fig. 1, "C," the lower uterine segment is permitted a degree of movement independent of these lower fascial attachments, thereby allowing it to move in conjunction with the body of the uterus and the fetus to adjust its long axis to the uterine cavity. In the case of an abnormal pelvis, the lower uterine segment at higher levels, not being fixed, can

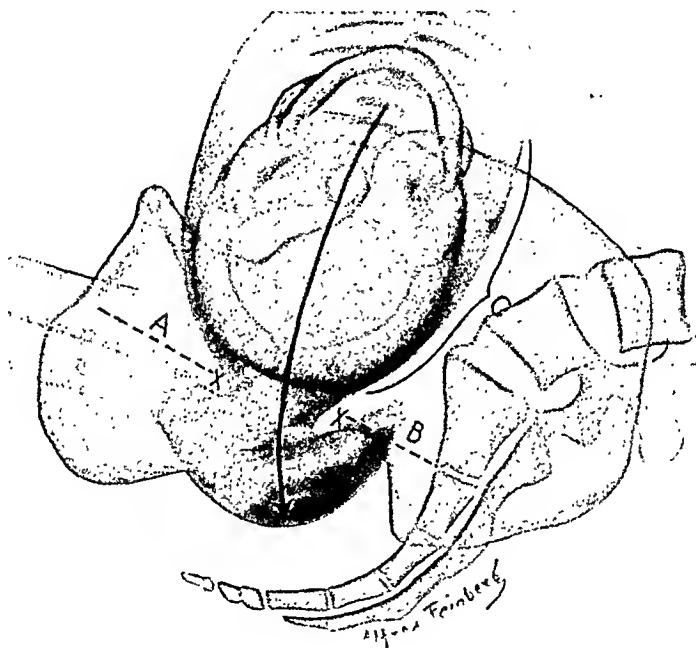


Fig. 1.—The lower uterine segment is outlined by 6 per cent sodium iodide which has infiltrated upward between the membranes and the lower wall of the uterus. Note the slight downward and backward axis of descent. Variations in the position of the axis of the lower uterine segment will result from differences in the lengths (A and B), strength, or character of the fascial supports originating from the utero-cervical junction at "X." The upper portion of the lower uterine segment "C" is freely adaptable to any particular fetal or uterine axis, and is flexible enough to allow fetal-pelvic adaptation to pelvic type at the inlet.

allow for any necessary adaptation from the standpoint of position in relation to the pelvis or asynclitism in relation to fetal piston axis. Thus, because of the freedom in movement possessed by the upper portion of the lower uterine segment, the fetus may be directed toward the inlet at practically any angle as a result of variations in the inclination of the pelvic inlet, variations in fetal piston axis, an inlet of abnormal shape, or the presence of relative disproportion.

Heretofore, obstetricians have placed considerable importance on these factors which modify the uterine axis in relation to the inlet.

Every conceivable method for measuring not only the bony pelvis itself, but also the inclination of the inlet as well, has been suggested without, however, supplying the full explanation of all the difficulties met. It is true that in certain individual cases labor may be prolonged by the presence of anterior or posterior asynclitism, but, as a rule, very early in labor these variable degrees of asynclitism are corrected, and the changing axis of the fetal head will indicate that the guiding influence of the lower uterine segment is making itself evident. Providing the uterine forces are strong enough, the head will follow an axis through the true pelvis, which is determined by this latter factor and not by the direction assumed by the fetal axis at



Fig. 2.—The first position of head after descent has occurred in labor. The head is descending through an axis in the fore-pelvis determined by the position of the lower uterine segment. Note the extreme flexion and molding. The anterior part of the head is close to the symphysis "A." Anthropoid type of pelvis. Position of head R. O. A. (Difficult medium forceps delivery, stillbirth.)

the inlet. By the time the cervix is partially dilated, the head in active labor will begin to assume the axis of the lower uterine segment, in which it will ultimately descend to the bottom of the pelvis. The guiding influence of the lower uterine segment and its fascial supporting structures continues to act in determining the axis of descent until the biparietal diameter of the head is in the fully dilated cervix. At this point the stretched fascial supports encircling the head exert their final influence. This terminal effect of the fully dilated cervix on the axis of the descending head can be observed when, prior to a forceps delivery, the last rim of the cervix is manu-

ally pushed over the head. As a result of this maneuver, the axis of the head may be rather suddenly deviated posteriorly from a forward direction.

(B) Variations in the Position of the Lower Uterine Segment

We have noticed that during labor, depending on the direction through which the fetal head is guided by the soft parts, three axes can be recognized. The following three illustrations from roentgenograms, taken after some degree of dilatation of the cervix had been at-

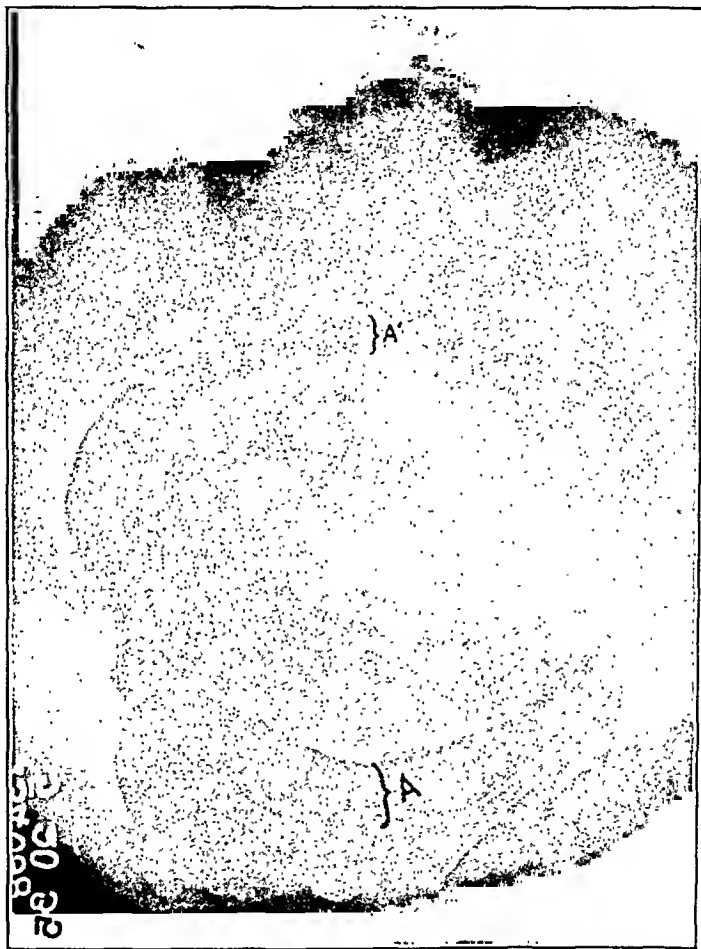


Fig. 3.—The second position of the head after descent has occurred in labor. The head is situated in the mid-axis of the pelvis, slightly favoring the posterior pelvis (Compare "A" and "A'.") Position of head L. O. T.

tained, are sufficiently characteristic to reveal the important points. For descriptive purposes these variable positions of the axes, along which the fetal head may descend late in the first stage of labor, may be classified the first, second, and third positions.

In the first extreme example (Fig. 2) the head is situated in the fore-pelvis with the anterior lateral aspect of the head close to the symphysis and descending pubic rami. The posterior lateral portion is considerably removed from the sacrum. Marked molding and flexion of the fetal head are also evident.

In the second position (Fig. 3), the head is centrally situated in the pelvis, theoretically equidistant from symphysis and sacrum, but, as a rule, the head while in this midposition actually tends to encroach more on the posterior pelvis.

In the third position (Fig. 4), the head is situated over the posterior pelvis with the anterior lateral aspect far removed from the symphysis and the posterior portion close to the promontory and sacrum.

These three extreme variations in position of the head may exist at the inlet, but at this high level the position is not of great signifi-



Fig. 4.—The third position of the head after descent has occurred in labor. The head is close to the promontory and sacrum, descending through the axis of the posterior pelvis, as determined by the position of the lower uterine segment. (Note distance from symphysis "A.") Position of head R. O. P.

canee. For instance, with the onset of labor the head from any position at the inlet may be forced downward and backward into the posterior pelvis according to the normal mechanism of labor. On the other hand, it may be forced to descend in an axis through the forepelvis; but only a trial of active labor will determine in which direction it will go. It is obvious that the subsequent mechanism in relation to the type of pelvis and the clinical course of labor will be modified by the particular axis of descent which the head is forced to follow.

In view of the fact that we believe the causative factor to be the supporting structures of the lower uterine segment, diagrammatic representations of the supposed appearance of these structures, which would deviate the head into the fore-pelvis or into the posterior pelvis after some measure of cervical dilatation has been attained, are illustrated in Figs. 5 and 6. While it is true that three degrees in the position of the pelvic axis can be recognized, from the standpoint of this investigation only the extreme forward and extreme backward

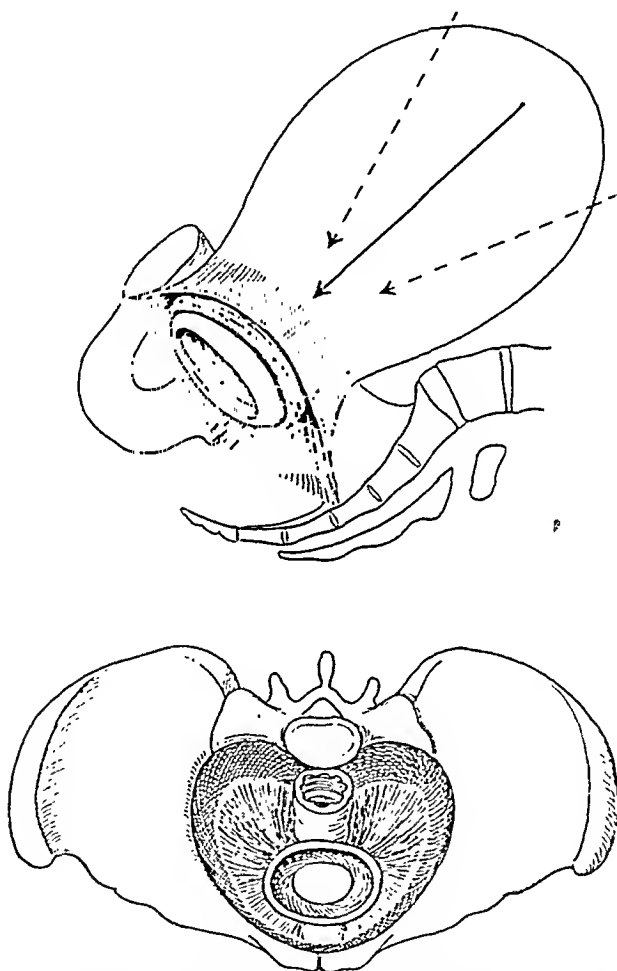


Fig. 5*.—Diagrammatic illustration to show the supposed position of the axis of the lower uterine segment in the fore-pelvis, as caused by the arrangement of the attachments of its fascial supports.

axis of descent are referred to, namely, the first and the third; and we shall now make reference only to the head descending in the fore-pelvis or in the posterior pelvis.

DESCENT OF THE HEAD THROUGH THE FORE-PELVIS

The head, which has descended into the fore-pelvis after partial or almost full dilatation of the cervix has been attained, may have origi-

*The diagrams shown in Figs. 5 and 6 do not indicate correctly the direction of the fascial attachment of the lower uterine segment. The proper direction of these supporting structures is shown in Fig. 1.

nated from such a range of position at the inlet that some attempt must be made to classify the various types and choose representative examples for illustration purposes. For discussion we have chosen the following case types:

1. The type of case in which the head is placed over the fore-pelvis at the onset of labor and descends through and adjusts itself to the particular shape of the fore-pelvis.

2. The type in which at the onset of labor the head is placed over the posterior pelvis where it has already adjusted itself to the particular shape of the posterior

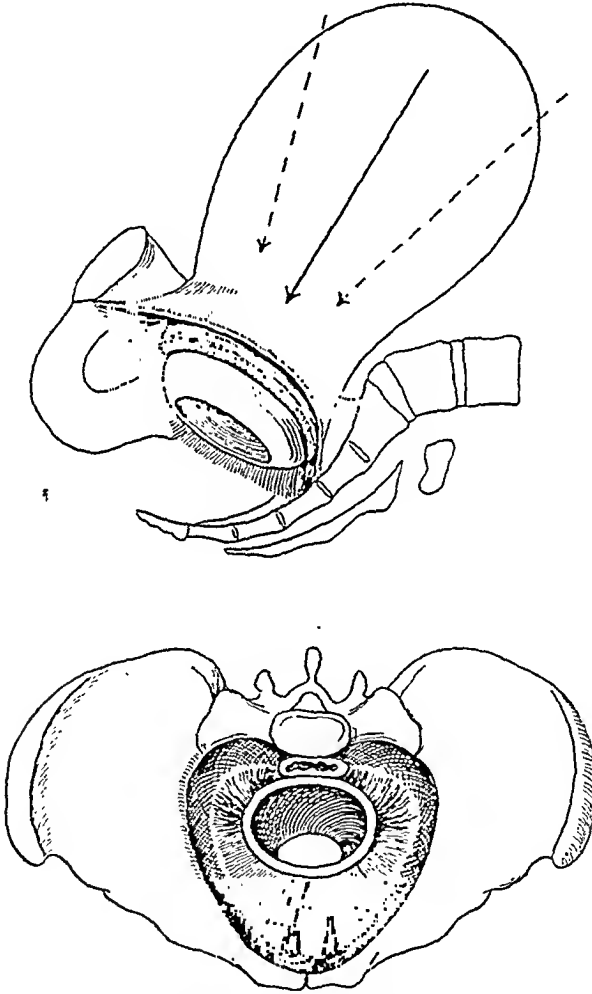


Fig. 6.—Diagrammatic illustration to show the supposed position of the axis of the lower uterine segment in the posterior pelvis, as caused by the arrangement of the attachments of its fascial supports.

segment, only to descend downward and forward during labor, readjusting itself to the shape of the fore-pelvis as it descends.

3. Example of a head directed into and descending through the fore-pelvis, even though the pelvis is normal with a normal inclination, and the child is average in size.

4. The high head in the fore-pelvis which fails to descend either through the fore-pelvis or through the posterior pelvis. Cesarean section ultimately becomes necessary.

(1) Descent and Adjustment to the Fore-Pelvis

We were especially fortunate in obtaining three stereoroentgenograms in the following case study, which demonstrate a number of characteristics of this particular type of mechanism. The type of pelvis corresponds to a fairly typical android with definite narrowing of the fore-pelvis at the inlet, slight convergence of the side walls, and

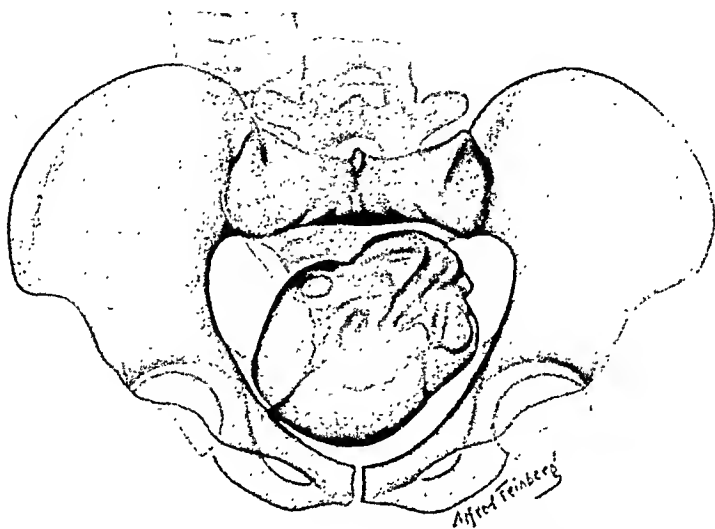


Fig. 7.—First x-ray examination in labor. Head descending through soft part axis situated in the fore-pelvis. Head position R. O. T. Type of pelvis typical android.

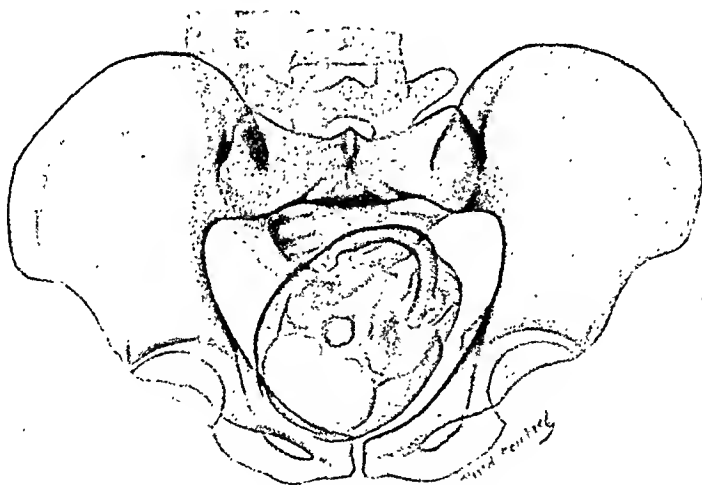


Fig. 8*.—Second x-ray examination in labor (same case as Fig. 7). Head descending through soft part axis situated in the fore-pelvis. The head has rotated to the R. O. T.-R. O. A. position.

slight narrowing of the subpubic arch. The first stereoroentgenogram early in labor shows the head over the fore-pelvis in the R. O. T. position (Fig. 7). A later x-ray study shows slight descent with the head now R. O. T. to R. O. A., still more in the fore-pelvis than in the posterior pelvis (Fig. 8). The last x-ray examination (Fig. 9) shows the

*In the succeeding half-tone illustrations with an x-ray effect, the ratio of head size to pelvic size has been modified to show to better advantage the axial position of head to pelvis.

head in the fore-pelvis close to the symphysis and descending pubic rami, almost in the direct O. A. position. When in this position the cervix was four fingers dilated, and the delivery was terminated from this position and level (at or slightly below the level of the spines) by low medium forceps. As a result of the downward and forward axis of the lower uterine segment, we find here an example of adjustment of the head to an anterior position in an android type of pelvis. We have a number of cases showing a pelvis quite similar to this one in size and shape, in which the head descended close to the sacrum in the O. T. position because the lower uterine segment directed the head through the posterior pelvis (see Fig. 17). In fact, this latter mechanism is the more common of the two. The demonstration of these two different mechanisms of labor, in regard to head position

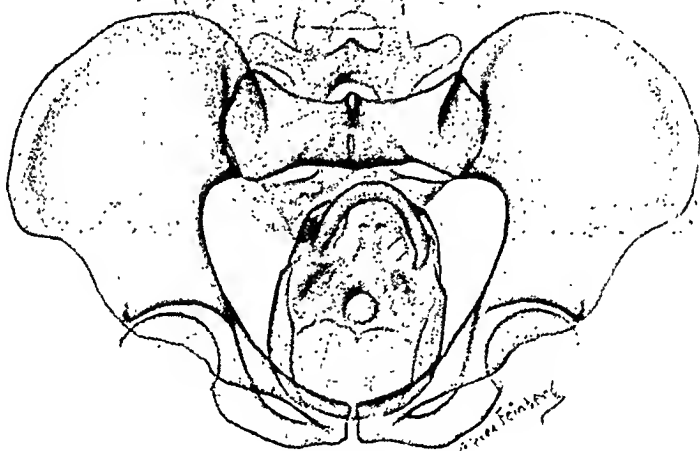


Fig. 9.—Third x-ray examination in labor (same case as Figs. 7 and 8). With further descent through the fore-pelvis the head has rotated almost to a direct O. A. position at the level of the spines.

during descent in the same type of pelvis, indicates the importance of the soft parts in labor. Thus a transverse position in an android pelvis can be predicted only on the basis that this is the more frequent mechanism. In the individual case, as illustrated in Figs. 7, 8, and 9, an anterior position may obtain if the head descends in the fore-pelvis.

Summary of Clinical Course of Labor in This Patient.—Mrs. J. F., white, primipara, aged thirty-five. Unit No. 266285. The patient was admitted to labor room at 7:40 A.M. March 27, 1936, with a history of ruptured membranes since 6 A.M. Pains started at 8 A.M. First x-ray examination at 11 A.M. (Fig. 7). Pelvic examination at 12:35 P.M. showed the cervix to be fingers II, thin, firm. Vertex R. O. T. in brim. Pains every three minutes, lasting thirty to forty seconds. Second x-ray at 4 P.M. (Fig. 8). Pelvic examination at 5 P.M. showed the cervix to be almost fingers III, dilated, thick and firm. Vertex now reported to be slightly anterior. Labor continued during night with pains of moderate intensity. In the

morning the patient was distended with gas. The uterus was deviated to the right. Pains poor in quality. Patient tired. Last x-ray examination at 8:30 A.M. (Fig. 9). Pelvic examination at 10 A.M. disclosed the vertex to be R. O. A. and showed the cervix to be fingers IV, dilated, and a thick rim remaining. Delivery by medium forceps at 4:47 P.M. March 28. Vertex direct O. A. in fore-pelvis at level of spines. Patient was in shock, requiring infusion and, several days later, a transfusion. Weight of child: 3430 gm. Duration of labor: thirty-four hours.

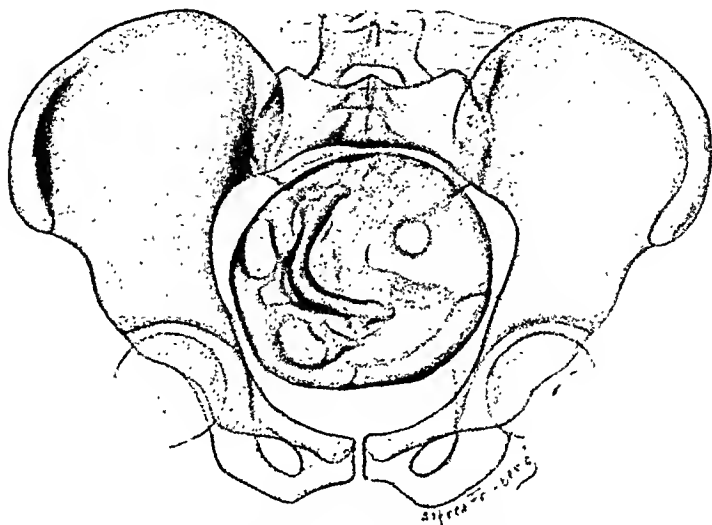


Fig. 10.—First x-ray examination early in labor shows vertex L. O. P. situated over posterior pelvis. Type of pelvis android with anthropoid characteristics.

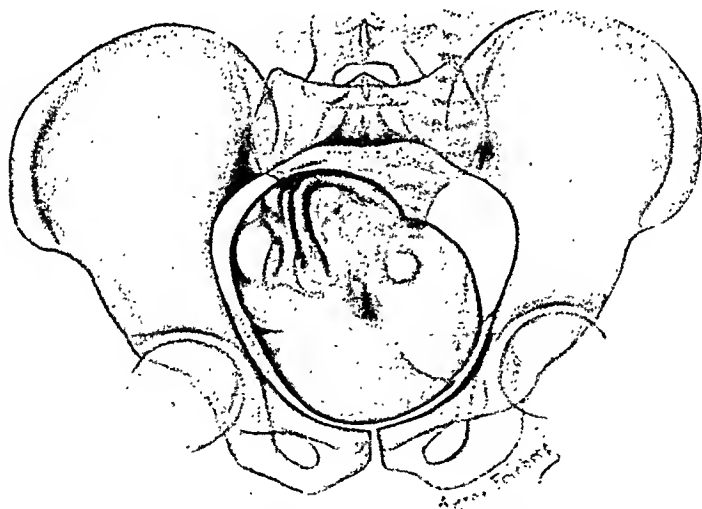


Fig. 11.—Second x-ray examination later in labor (same case as Fig. 10). The fetal head has been carried forward and downward into the fore-pelvis by the influence of the position of the lower uterine segment. As it is carried into the fore-pelvis, close to the symphysis, it has adapted itself to the narrow fore-pelvis by rotating to the L. O. A. position.

(2) *Descent Through Fore-Pelvis From a Primary Posterior Pelvis Position at the Inlet*

We have a number of case studies to illustrate this interesting type of axis of descent through the fore-pelvis and its resultant effect on the mechanism of labor in relation to pelvic type. The pelvis conforms

to the android type with anthropoid characteristics, in which definite transverse narrowing exists throughout the pelvis and a long, narrow fore-pelvis is present. The first roentgenogram (Fig. 10) obtained in labor showed the head engaged in the L. O. P. position and situated over the posterior pelvis. This is the ideal position for the head at the inlet in this particular type of pelvis. The second roentgenogram obtained in labor, however, shows a very different fetal-pelvic relationship (Fig. 11). The head is now close to the symphysis and pubic rami, far removed from the mid and lower sacral region in the L. O. A. position. In other words, the head has descended downward and forward along an axis which carries it away from the posterior pelvis into the fore-pelvis and so prevents it from utilizing the maximum space posteriorly. Normally, such deviation of the axis anteriorly should not occur until the head has passed through the

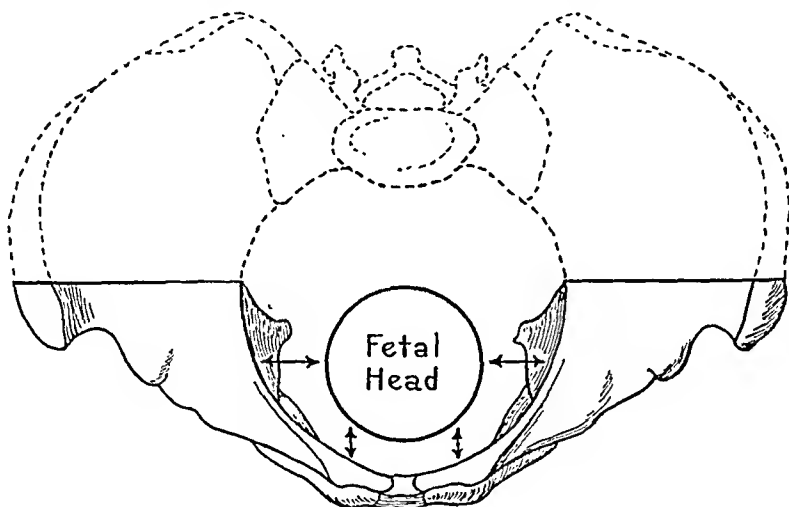


Fig. 12.—Diagram to illustrate that a head carried through the fore-pelvis by virtue of a forward axis of the lower uterine segment will attempt to adjust itself to the shape of the bony boundaries of the fore-pelvis.

cervix. To compensate for this change in axis of descent, the head must now adapt itself to the shape of the bony walls of the fore-pelvis.

Clinical Course of Labor.—Mrs. K. C. (Unit No. 448977), white, primipara, aged twenty-four. Weight of baby: 3600 gm. The patient was admitted at 6 A.M. July 2, 1935, with a history of uterine contractions since 3 A.M. The vertex was engaged on admission. Pains increased in frequency and severity. First x-ray examination at 9:20 A.M. (Fig. 10). Pelvic examination at 11:30 A.M. revealed a narrow rim of cervix remaining; membranes ruptured. Position L. O. T. The head was pushed against the symphysis with plenty of room in hollow of sacrum. Second x-ray examination at noon (Fig. 11). The labor was terminated at 3:30 P.M. by low medium forceps after failure to advance with adequate second stage contractions. Duration of labor: twelve and one-half hours.

We believe these two case studies (Figs. 7 to 11) demonstrate certain principles in regard to fetal head adaptation during descent as

well as in the variation in the pelvic axis through which the fetal head descended. The principle, to a certain extent, is illustrated in Fig. 12, which indicates that when a fetal head is forced to descend through the fore-pelvis it must attempt to adjust itself to the particular shape of the fore-pelvis. We have a number of similar examples, in which the head adjusted itself during labor from some other position at the inlet to a direct O. P. position lower in the fore-pelvis as it was guided downward and forward through the axis of the lower uterine segment. In such cases, the pelvis usually conforms to an anthropoid type with a narrow fore-pelvis.

(3) *Fore-Pelvis Descent Through a Normal Pelvis*

The case studies just described possessed pelves of abnormal size and shape, and as a result the pelvis itself may be supposed to have

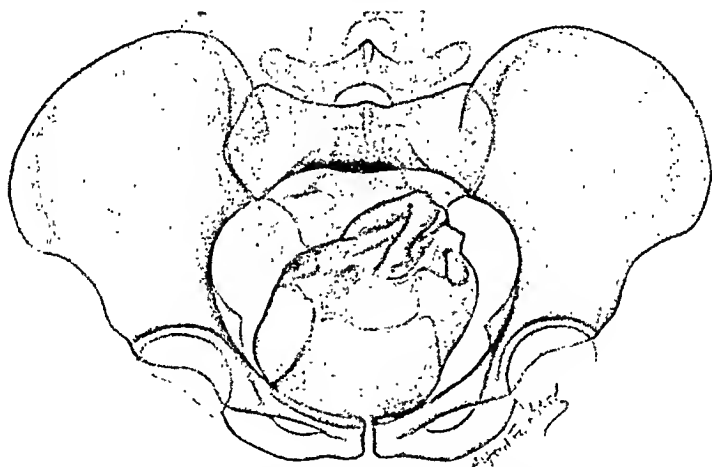


Fig. 13.—A good example of a head directed downward and forward by the lower uterine segment against the symphysis into the fore-pelvis. The pelvis is normal. No fetal-pelvic disproportion is present. The inclination of the pelvis is normal.

modified the course of the head in association with a downward and forward fetal piston axis. We were fortunate in obtaining the example shown in Fig. 13, which would seem to give further support to the theory that the position and direction of the axis of the lower uterine segment is determined by its fascial attachments to the pelvic side walls. The pelvis conforms to the normal or gynecoid type. The inclination of the inlet is normal. The roentgenogram illustrates that the anterior parietal aspect of the fetal head is quite close to the posterior aspects of the symphysis and that a large space exists between the posterior lateral aspect of the head and the lower sacral region. It is true that the axis of the fetus is pointing downward and forward, and, theoretically, such an attitude might be regarded as the sole cause for the position of the head in relation to the pubes. It is hard to believe, however, in a pelvis of such ample dimensions that fetal

axis alone would prevent the head from making use of the spacious posterior pelvis. The labor was prolonged and complicated by inertia and slow cervical dilatation. The delivery was terminated by a low medium forceps operation.

Clinical Course of Labor.—Mrs. F. B. (Unit No. 476830), white, primipara, aged thirty-four. Weight of child: 3550 gm. Length of labor: twenty-seven hours. The patient was admitted to labor room at 8:30 P.M. Aug. 11, 1936, with history of pains since 12:15 A.M. Pelvic examination at 11:15 P.M. shows the cervix to be fingers II, dilated and thin. Vertex near spines, R. O. T.; membranes ruptured. Moderately severe contractions continued during the night and the following morning. X-ray (Fig. 13) examination was obtained about 10 A.M. August 12. Pelvic examination at 1:15 P.M. showed the cervix to be fingers III to IV, dilated. The anterior lip of the cervix was firm. Vertex in fore-pelvis (No. 1 position) R. O. T. Marked caput

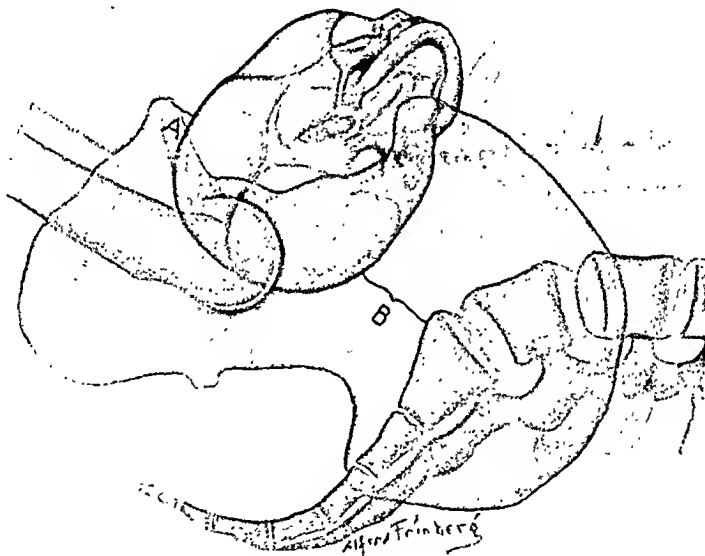


Fig. 14.—X-ray examination obtained during trial of labor. Head is high, held against symphysis. (Compare the lengths of A and B with similar distances shown in Fig. 19.) Cesarean section.

and molding at level of spines. Pains occurring every two or three minutes. With cervix out of the way and the vertex R.O.T., the patient was delivered by low medium forceps at 5:20 P.M.

(4) *The High Head in the Fore-Pelvis Which Fails to Descend*

A study of the roentgenograms obtained during a trial of labor, in which the delivery was accomplished later by cesarean section, illustrates several important points which may or may not be attributed to the position of the lower uterine segment. In Fig. 14 the head is high over the fore-pelvis close to the symphysis and abdominal wall. It is true that there is disproportion in conjunction with an abnormal pelvis in this case, but, from our own clinical experience, we believe that this high head, to a certain extent, is held forward by tense fasciae which

maintain the head in a poor mechanical situation for descent and that, had the same head in the same pelvis been permitted to occupy a position over the posterior pelvis at the beginning of labor, delivery from below might have been possible.

We have pointed out that the upper portion of the lower uterine segment is not controlled by fascial attachments to the same degree as its lower portion (Fig. 1). To assume that tense fasciae may hold a floating head against the symphysis at the inlet would require an associated high level for the uterocervical junction ("X," Fig. 1), from which the supporting structures originate.

From these observations it would seem that such variations in the level of the cervix must exist, due to the fascial supports themselves; but further investigation is necessary to prove this point.

DESCENT THROUGH THE POSTERIOR PELVIS

As in the analysis of examples of descent through the fore-pelvis, case studies can be found to demonstrate great variation in the extent to which the fetal-pelvic relationship must change before the head ultimately descends in a posterior axis in relation to the sacrum and shape of the posterior pelvis. Comparable types of cases discussed under descent through the fore-pelvis may be chosen.

1. Descent from inlet to outlet through the posterior pelvis and associated adjustment to the shape of the posterior pelvis.
2. Descent through the posterior pelvis from a primary position high over the fore-pelvis.
3. The efficient course of labor in normal pelvis, with a child of average or under average size, when descending through the posterior pelvis.
4. The favorable prognostic sign of a head high, but situated over the posterior pelvis.

(1) Descent From Inlet to Outlet Through the Posterior Pelvis

The shortest and easiest axis for the head to follow when situated at the onset of labor over the posterior pelvis is that through the posterior pelvis. An example has already been given in Fig. 4, where it will be observed that the fetal head is descending in a large anthropoid type of pelvis in the R. O. P. to R. O. T. position, close to the promontory and sacrum. The labor was uncomplicated, except for an outlet forceps delivery. Precisely the same axis is being followed in the example shown in Fig. 15. The pelvis in this case conforms to the typical android with a gynecoid fore-pelvis. The head, revealing extreme flexion and molding, is descending in the R. O. T. to R. O. P. position, close to the sacrum and as far removed from the posterior aspect of the symphysis as it is mechanically possible to be. In this case, in spite of a large child (8 pounds) and a small abnormal pelvis,

the vertex descended rapidly through the pelvis to bulge the posterior perineal region. After failure to advance beyond this low level, labor was terminated by forceps. Under these circumstances the influence



Fig. 15.—Anteroposterior roentgenogram showing the head, R. O. P.-R. O. T. position, descending through the posterior pelvis as far removed as possible from the symphysis, A. Type of pelvis android.

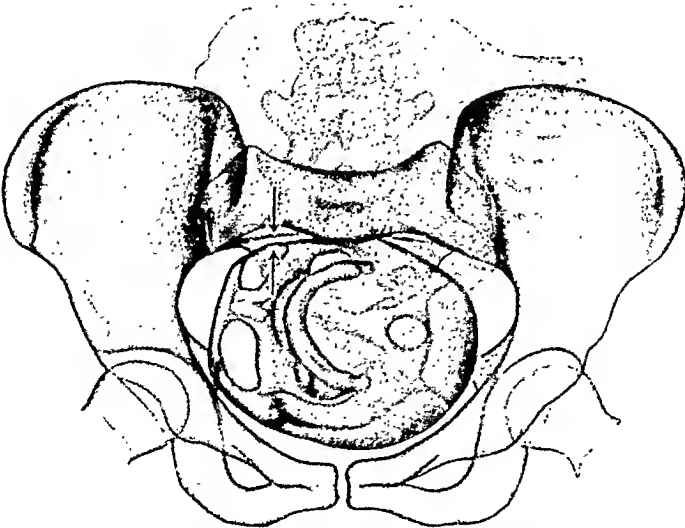


Fig. 16.—Mechanism in the android type when the head is directed through axis of the posterior pelvis. The head is in the O. T. position and, as a rule, maintains this position to a low level as a result of the shape of the posterior pelvis.

of the type of pelvis upon head position during descent through the posterior pelvis becomes apparent. In other words, when the head is

forced to follow the axis of a lower uterine segment situated in the posterior pelvis by virtue of the length, strength, and character of its fascial supports, the head will attempt to adjust itself to the shape of the posterior pelvis as it descends (Fig. 16).

Last year we discussed this particular result on the mechanism of labor and described the mechanism in android types according to the principles illustrated in Fig. 17. In anthropoid types, when the head engages and descends in the oblique posterior position through the axis of the posterior pelvis (Fig. 4), rotation to the anterior position usually does not occur until the head is through the cervix and meets the resistance offered by the lower posterior aspect of the pelvic gutter. Thus when we observe the head descending in the posterior pelvis, the type of which is known, we can understand the reasons for expecting transverse positions in android types, and posterior positions in

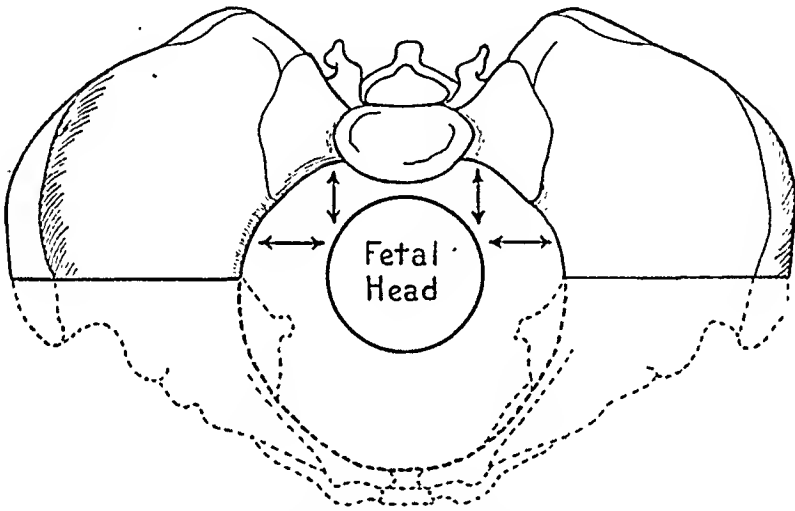


Fig. 17.—Diagram to show that, if the head is directed through the posterior segment of the pelvis by the position of the axis of the lower uterine segment, it will adjust itself to the shape of the posterior pelvis. Hence, transverse positions are common in android types, and posterior positions in anthropoid types.

anthropoid types; and we can also understand why, as a result of fetal-pelvic adaptation to the shape of the posterior pelvis, the head may not be rotated at the level of the spines with ease in the android type, but must be brought to a lower level before rotation can be effected; or why in the anthropoid type of pelvis the posterior position may be difficult to rotate until it has descended through the cervix.

(2) *Descent Through the Posterior Pelvis From a Primary Position High in the Fore-Pelvis*

In contrast to cases of descent through the fore-pelvis from a primary position higher in the posterior pelvis, we have encountered examples in which the head was originally directed into the fore-pelvis, but later in labor was forced to descend in an axis determined

by the axis of the dilating lower uterine segment, which showed a downward and backward curve. A representative example is shown in Figs. 18 and 19. Early in labor (Fig. 18) the head presented high, close to the symphysis in the L. O. T. position, with a definite posterior parietal tendency and with the long axis of the fetus directed downward and forward. The second x-ray examination, obtained when the

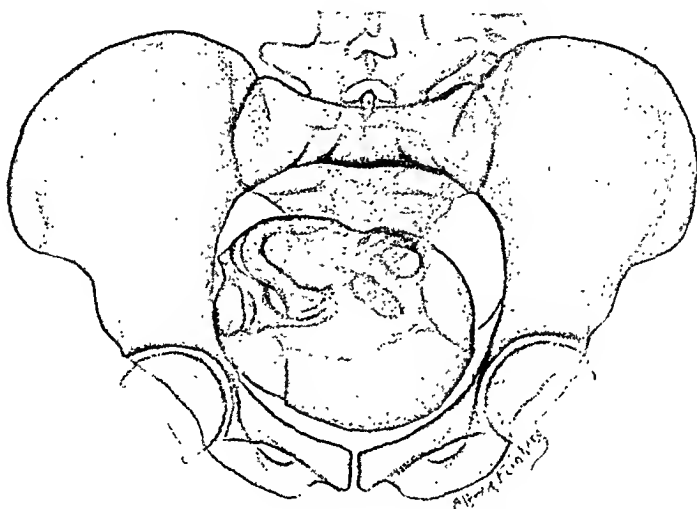


Fig. 18.—X-ray examination early in labor. Vertex L. O. T. posterior parietal position situated over fore-pelvis.

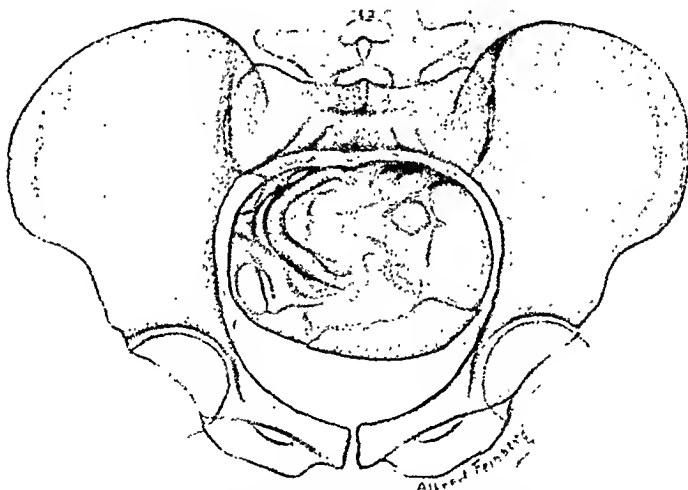


Fig. 19.—Second x-ray examination later in labor (same case as Fig. 17) shows vertex has been carried away from symphysis into the axis of posterior pelvis by means of the influence of the lower uterine segment.

cervix was fingers III to IV, dilated (Fig. 19), shows that the downward and forward axis of the fetus, as a whole, still persists, although to a lesser degree, and that the entire head is now more removed from the symphysis and is situated nearer to the posterior pelvis. A long labor was necessary to permit the head to descend slowly, more and more into the axis of the lower uterine segment situated in the posterior pelvis. Because of lack of satisfactory progress the patient was

placed on the delivery table with the cervix thinned out and four fingers dilated. As soon as the bi-parietal diameter of the head passed through the cervix, it laterally flexed into the posterior pelvis close to the sacrum in its proper axis for further descent.

Clinical Course of Labor.—Mrs. A. M., white, primipara, aged twenty-three. Weight of child: 3270 gm. Duration of labor: fifty hours. The patient was admitted to the labor room at 11:30 P.M. Sept. 10, 1935. Pains began at 10 P.M. with slight show. On admission contractions occurred every fifteen to twenty minutes, lasting thirty or forty seconds. Pelvic examination at 10:30 A.M. showed the cervix to be fingers I dilated, thick, effaced. First x-rays at 10:50 A.M. (Fig. 18). Pains increased in frequency. Pelvic examination at 1 A.M. September 12 showed the cervix to be fingers II dilated and thick; membranes intact. Pelvic examination at 9 A.M. September 12 showed the cervix to be fingers IV. Second x-ray examination at 10 A.M. September 12 (Fig. 19). Pelvic examination at 11 A.M. revealed the cervix to be thin, and fingers IV dilated. Delivery by low forceps at 2:57 P.M. September 12. Head at spines, vertex L. O. T. Sagittal suture pointing into the fore-pelvis. Thin rim of cervix. As the cervix was pushed over the head the vertex laterally flexed into the posterior pelvis and was rotated manually at a lower level to an O. A. position.

(3) *The Efficient Course of Labor in a Normal Pelvis With Descent Through the Posterior Pelvis*

In a recent publication¹ we discussed fully the normal mechanism of labor and pointed out that the head normally is directed downward and backward, more through the posterior pelvis than through the mid- or fore-pelvis. As a result of the soft parts directing the head more commonly in this posterior axis, we were able to associate anatomically this common soft part axis with the bony pelvis. For practical purposes this soft part axis corresponds to a line descending parallel with the sacrum from the points of intersection of the widest transverse diameter and the anteroposterior diameter at the inlet. Although labor, as a rule, is efficient when such an axis is followed, a number of exceptions have been noted in which the labor is complicated by inertia and cervical dystocia, and an operative delivery may become necessary. We have observed that at the onset of labor the head may have already descended to a low level in the pelvis in an ideal axis for further descent in the axis of the posterior pelvis. Such a case is illustrated in Fig. 3. Yet, during labor, the cervix dilated slowly and inertia was present. The delivery was terminated by manual dilatation of the cervix and a low median forceps operation. The presence of a normal pelvis and engagement of the head in similar examples rule out the possibility of disproportion. This type of case is not uncommon. We have observed, however, that the head is frequently large and round. The explanation for the cause of the diffi-

culty with the cervix is not clear, but it would seem that the fascial supports, although maintaining the head in a good position, prevent it from effectively distending the lower uterine segment to "get at the cervix."

(4) *The High Head Held Over the Posterior Pelvis as a Favorable Prognostic Sign*

Occasionally the floating head causes considerable concern early in labor, whether or not the patient is known to have a normal or abnormal pelvis. If, however, it is held close to the sacral promontory, as illustrated in Fig. 20, a longer trial of labor is justifiable, because it is situated over the posterior pelvis in an ideal position for descent,

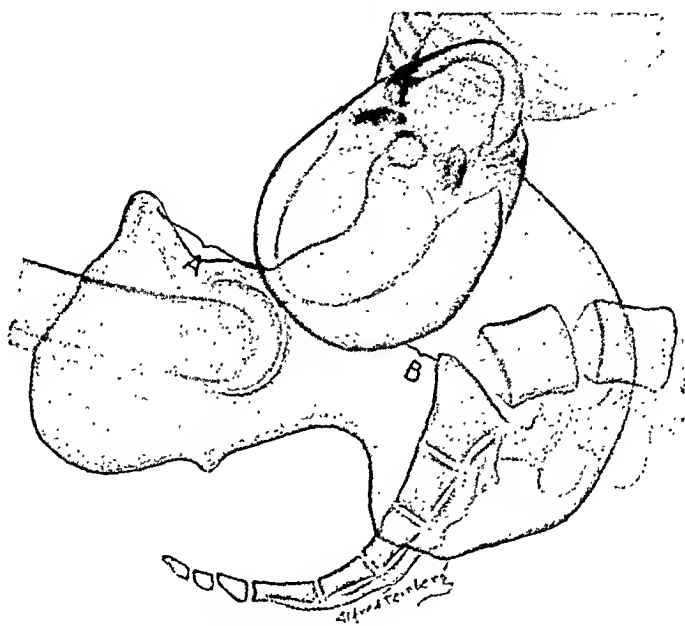


Fig. 20.—The fetal head, though floating, is situated close to promontory over the posterior pelvis in the ideal position for descent through the posterior pelvis. Favorable prognostic sign. (Compare the lengths of A and B with similar distances shown in Fig. 14.)

provided, of course, the soft parts are so disposed as to maintain this axis throughout the posterior pelvis as the head descends.

FREQUENCY OF OCCURRENCE OF THESE VARIATIONS
IN AXIS OF FETAL DESCENT

In view of the fact that considerable experience is necessary on the part of the observer in order to appreciate correctly, in the stereoscopic image of head and pelvis, the axis of fetal descent in relation either to the symphysis in front or the sacrum behind, we considered at one time that the descent through the fore-pelvis was rare in occurrence, and that in the vast majority of all cases the descent was eventually through an axis in the more ample posterior pelvis. However, when

we reviewed films obtained during the investigation of related aspects of the mechanism of labor and became more experienced in the study of fetal-pelvic relationships, we began to find that varying degrees of descent through the mid- or fore-pelvis occurred with greater frequency than we had suspected.

At this time, however, we have made no statistical analysis of our series possessing one or more stereoroentgenograms obtained in labor, and we hesitate to suggest the frequency with which the head may be directed downward through the fore-pelvis. Yet, it is of sufficiently common occurrence to be taken into account in each case of prolonged labor, because, as the histories indicate, the clinical course of labor in these cases appears to be complicated by inertia, cervical dystocia, and prolonged labor. Manual dilatation of the cervix, followed by a forceps delivery, is not an uncommon method of terminating the labor in these cases.

In conclusion, although the roentgenologic and clinical data must be correlated with great care in a larger series of cases, we believe that a knowledge of the axis of descent is essential before the proper treatment can be instituted. Earlier recognition of these variations in labor by either roentgenologic or clinical methods of diagnosis, or both, will enable us to institute the proper treatment early in labor, in an attempt to avoid exhaustion of the patient and the difficult operative deliveries which are so frequently necessary in these cases.

SUMMARY

1. The lower uterine segment and its fascial supports represent an active force in determining the axis along which the fetal head must descend through the pelvis.

2. The maximum guiding influence of the lower uterine segment becomes evident only after definite dilatation of the cervix has occurred.

3. The position of this axis is variable in each individual case, and examples of descent through the fore-pelvis, the mid-pelvis, and the posterior pelvis are described.

4. The clinical course of labor and the head position in relation to pelvic type is distinctly modified, depending on the particular axis the head follows.

5. In the majority of instances, roentgenologic diagnosis cannot be made dogmatically during labor, because only the active forces of labor can ultimately determine the axis through which the head can descend. The later the examination is taken, the greater the possibility of accurately determining the axis the head is attempting to follow.

6. These variations in labor in the fetal axis of descent, we believe, will ultimately enable us to understand the question of inertia and cervical dystocia, and the correct method of treatment for these conditions.

7. A knowledge of the possible occurrence of these variations in any individual case in labor is essential before a reliable clinical and roentgenologic diagnosis can be made.

8. Patients who are not progressing normally in labor warrant a careful examination in order to determine, among other things, if the head is descending in the proper relation to the symphysis in front or the sacrum behind.

9. The variability of the fetal axis of descent with its resultant effect on the mechanism of labor indicates that difficulty in labor cannot be anticipated by linear or volumetric measurements alone.

10. The mechanism of labor in relation to the shape of the pelvis cannot be adequately discussed without taking into account the variations in the position of the axis of the lower uterine segment, along which the head descends.

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875 PARK AVENUE

DISCUSSION

DR. E. D. PLASS, IOWA CITY, IA.—I must confess that I find some difficulty in following the arguments of the authors.

It is quite easy to agree with the first point brought forward, namely, that the posterior parietal bone presents earlier than the anterior, but I am inclined to believe that such a phenomenon is associated with some distortion of the bony pelvis rather than with abnormalities of the soft parts. It is obvious that if the pelvic inclination is increased, there would be a tendency for the posterior parietal to descend first, and we have long recognized that in patients showing even slight disproportion there is a tendency in the same direction. I find it very difficult to think of soft tissues altering the position of the head and am rather inclined to the opinion that the position of the soft parts, that is of the lower uterine segment, is more likely to be determined by the configuration of the bony canal. There are several arguments that seem to support such a contention. For example, it is recognized that a patient with unilateral lameness has probably a distortion of the pelvis with one oblique diameter longer than the other, and it has been almost a universal experience that the head enters the pelvis in the long diameter. The head accommodates to the change of the bony pelvis irrespective of the soft parts.

Some of the slides that Dr. Caldwell has shown are difficult to interpret because of the lack of definite knowledge as to the situation of the head. I gathered the impression that the distance between the head and the symphysis may well depend upon the situation of the head; that as the head is engaging it might have come

closer to the sacrum or to the symphysis, whereas after descending into the pelvis there would be a tendency for closer approximation to both the anterior and posterior walls.

The arguments that were advanced in the paper, but were not included in the spoken presentation, concern in part the possible activity of the uterosacral ligaments and I gained the impression from going over the manuscript that Dr. Caldwell feels that those ligaments are contractile in nature. The general teaching is that the uterosacral ligaments are merely folds of connective tissue, and that being the case, it is difficult to understand how they can in any way actively influence the position or shape of the lower segment and thus influence the position in which the baby enters the pelvis.

There has developed a fairly wide appreciation of the fact that under the influence of the changes induced by pregnancy all malpositions of the uterus, including both the cervix and the body, tend to disappear. We are familiar with the fact that the retroverted pregnant uterus usually cannot be differentiated in three or four months from the uterus that started pregnancy in the anteverted position. That susceptibility of the uterus to alterations in its position makes me very skeptical of its having such influence upon the position of the head during labor.

DR. ALBERT H. ALDRIDGE, NEW YORK, N. Y.—At the Woman's Hospital we have had no actual experience in studying the mechanism of labor by the Caldwell method. However, I would like to call attention to certain commonly observed facts which seem to suggest that it is almost impossible, during labor, for the fascial supports of the uterus so to fix the position of the lower uterine segment in the anteroposterior diameter of the pelvis, as to constitute an important factor in directing the course of the fetal head.

From the anatomical standpoint, it is agreed quite generally that the uterus is supported by a layer of endopelvic fascia referred to as the upper pelvic floor. In the base of each broad ligament this fascia is thickened to form the so-called cardinal ligaments which are attached to the uterus at the level of the internal os. These ligaments extend laterally and provide the chief support for the uterus. That portion of the endopelvic fascia extending between the uterus and the inner surface of the anterior border of the pelvis is looked upon as the weak portion. Posteriorly the upper pelvic floor is composed of a layer of endopelvic fascia and the uterosacral ligaments.

Undoubtedly, as Dr. Caldwell has pointed out, the position of the cervix in relation to the sacrum and symphysis pubis varies slightly in different women. If the cervix were held in this fixed position, during labor, it is conceivable that it might be a factor in directing the course of the fetal head.

It is known that any relaxation of the endopelvic fascia supporting the uterus, and especially the cardinal ligaments, results in great mobility of the uterus and in some degree of uterine prolapse. When the cardinal ligaments are shortened, even as little as $1\frac{1}{2}$ to 2 cm., on either side, by the Donald-Fothergill operation, a prolapsed uterus, with cervix presenting at the vaginal introitus, can be restored to a normal position.

As the cervix dilates at the level of the internal os during labor, it is obvious that the fascial supports of the uterus which are attached at this level must relax, allowing increasing mobility of the lower uterine segment. When the cervix has reached full dilatation, it practically lines the true pelvis, causing complete relaxation in every direction of all the fascial supports of the uterus, allowing great mobility of the lower uterine segment. This undoubtedly is nature's protective mechanism which prevents injury of the fascial supports of the uterus during labor.

At the end of the third stage of labor, there is so much mobility of the uterus that the cervix frequently presents at or protrudes through the vaginal introitus. If under such circumstances the uterus is replaced manually to a normal level, it will

be found that the cervix can be easily moved to any position in the true pelvis. As the cervix closes during involution, normal tension is restored to the fascial supports of the uterus. As a result, a uterus which seems definitely prolapsed at the end of labor will invariably be found in normal position when involution is completed.

Therefore, in view of the facts presented, it seems doubtful as to whether the lower uterine segment remains sufficiently fixed in position, as labor progresses, to constitute an important factor in directing the course of the fetal head.

DR. HUGO EHRENFEST, St. Louis, Mo.—Caldwell's careful x-ray observations have established marked variations in the proximity either to symphysis or sacrum of the axis along which the head descends into the pelvis. According to his view, the unfavorable approach toward the symphysis on the one hand, and the more favorable deviation of the head backward toward the sacrum on the other, are determined by certain anatomic conditions of the fasciae supporting and stabilizing the cervix. It seems to me that his contention is well supported by certain observations we make in vaginal examinations, during labor. We find in one case the dilating os close to the symphysis with a broad, distended posterior cervical lip, and discover in another case just the opposite situation with the os far back in the posterior fornix. If I understand the essayist correctly, these variations would have to be considered to be of great prognostic significance.

I am wondering whether Dr. Caldwell, on the basis of his information concerning the fixation of the cervix in relation to either the anterior or the posterior pelvic wall, is willing to support my own idea of the occasional fixation of the cervix at an unusually high level in the pelvis. I assume this condition to be present when in a primigravida with a normal pelvis, a seemingly normal, flexed head fails to become engaged either late in pregnancy or even with beginning cervical dilatation in labor. We all have observed cases in which such an unengaged head with complete dilatation of the cervix and rupture of the membranes rather quickly descends into the pelvis. Many an unjustifiable cesarean section has been done under such conditions, because failure or rather impossibility of the head to enter the inlet had erroneously been ascribed to a disproportion.

DR. LILIAN K. P. FARRAR, New York, N. Y.—The supports of the uterus have received many different names, "the parametrium," "the broad ligaments," "the cardinal ligaments," "the sustentacular apparatus" of Bonney, and perhaps the most inclusive name, "the upper pelvic floor" by Polls. The best description, however, I believe, is that given by Maackenrodt in 1894 ("ligamentum transversalis colli"), who described a triangular wedge of tissue on either side of the cervix made up of thick bundles of muscle and connective tissue passing from the sides of the pelvis into and down the sides of the cervix and vagina and extending anteriorly from either side of the rectum up to and under the bladder. This "ligament" Maackenrodt held to maintain the uterus in ante flexion. I believe that Dr. Caldwell is correct in assuming that these fascial attachments of the lower pole of the uterus influence the fetal head in its descent through the pelvis.

DR. BENJAMIN P. WATSON, New York, N. Y.—I would like to say that Dr. Caldwell and his associates are approaching this subject in a most critical fashion. I have been one of their chief critics. Their evidence is becoming so great in the type of pelvis to which Dr. Caldwell has applied these investigations that I am a convert to the idea that the soft parts do play a considerable part in a great many dystocias.

DR. CALDWELL (closing).—The mechanism of labor as shown in the first slide is the usual mechanism which we have found in a very careful and rather critical examination of over 250 primipara cases. It is very difficult to see what else would tilt the child's head toward the symphysis or carry it backward toward the center of

the pelvis except the shape and the support of the lower uterine segment. It is difficult to see a very small head held close to the sacrum in a very large anthropoid pelvis where we cannot find any bony obstruction and explain it on a basis of bony disproportion. Undoubtedly bony disproportion would hold the head up, but in the cases where x-ray shows no bony disproportion it is difficult to explain it in any other way except by the soft parts. A great many cases that are held close to the symphysis dilate the cervix up to two or three fingers' dilatation and on rectal examination you can find a good deal of space between the posterior parietal bone and the sacrum, and with each drive it is pushed forward into the pelvis. Ultimately this is corrected and in subsequent pregnancies the labor must be very much easier. It would be well if the Society would investigate this subject during the coming year and see whether we are right or not.

A CLINICAL REVIEW OF 110 CASES OF OVARIAN CARCINOMA*

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THE diagnosis of tumors is not always easy. It is one thing to outline the mass but quite another matter to determine its nature when the patient is difficult to examine, or complications are present. A review of tumors treated recently in my clinic showed that 5.6 per cent of 300 fibroids were not recognized as such preoperatively, nor were 15 per cent of 302 ovarian neoplasms recognized as ovarian. Follicle and corpus luteum cysts were not included in the group because they are not true neoplasms. In addition to these errors, there were at least as many "correct and incorrect" diagnoses, which term we used when a fibroid or ovarian cyst associated with some other pelvic condition was present and diagnosed but the associated condition was not, or when the likely possibilities of the mass alone were listed with arguments for and against each proposal, but without definite conclusions. The net result of this study showed an absolutely correct diagnosis in less than 90 per cent of 300 fibroids, and in only 64 per cent of 302 true ovarian neoplasms.

The importance of determining the exact nature of any tumor preoperatively needs no discussion. Thirty-six per cent of the 302 ovarian neoplasms under study proved carcinomatous, while cancer occurred in the uterus or tumor in two and a half per cent of 1,200 fibroids. Errors in diagnosis of ovarian tumors assume added importance because the improvement in results attending the present-day treatment of cervical cancers and of cancers of the uterine body has not yet been obtained with ovarian carcinoma. These reasons influence me to pre-

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 28, 1936.

A study made possible by the Cancer Fund of the University of California.

sent this clinical review of 110 ovarian cancers, all of which have been followed from treatment to death or to a survival as long as nineteen years.

MATERIAL

The material consists of 110 proved carcinomas, all primary growths, except two Krukenberg tumors. Excluded from this series are several carcinomas which were secondary to cancer primary in the uterus, also several secondary sarcomas.

The series comprises 95 papillary and/or adenocarcinomas, 5 malignant pseudomucinous tumors, 1 squamous cell carcinoma arising in a dermoid, 1 dysgerminoma, 6 granulosa cell tumors, and the 2 Krukenberg tumors which were considered primary ovarian tumors before operation, and gave no clear history of the stomach cancer until after the tumors had been removed. Sixty-five of the entire group were bilateral, and 45 were unilateral tumors. Checkup of the histories of the 45 unilateral tumor patients showed that one ovary had been removed by operation in nine of them a few years before the beginning of the present illness. Sixty of the papillary and adenocarcinoma group were double, and 35 were unilateral tumors. Two dermoids were found in ovaries which were the seat of adenocarcinoma. These dermoids, however, were not involved in the malignancy.

The 110 ovarian carcinomas constituted 36 per cent of 302 ovarian neoplasms, 13.3 per cent of 825 pelvic cancers in women, and 4.8 per cent of 2,300 pelvic neoplasms treated in the University of California Hospital from 1916 to date. The microscopic findings in 17 of the papillary adenocarcinomas indicated that they originated in a previously benign papillary adenoma. All of them contained areas which showed irregular proliferation of epithelial cells, mitotic figures, hyperchromatism, obvious invasion of the stroma, and round cell infiltration surrounded by areas of benign tumor formation. To these 17 malignant cases we must add another, although the microscopic findings indicated that it was benign. It recurred, however, a few months after what was considered a complete removal of the tumor, the opposite ovary, and the uterus. Nor did it regress after roentgen ray therapy but caused ascites and death within sixteen months.

FAMILY HISTORY

The part that inheritance of susceptibility to cancer (or failure to inherit resistance to it) plays in the etiology of cancer is a moot question which cannot be proved or disproved at present, either by clinicians or by eugenicists, who are as divided in their opinions as we are ourselves.

Cancer now is the second most common cause of death noted in Bureaus of Vital Statistics. Accordingly, patients when intelligently questioned should report cancer in their family history, provided the medical history of many of their blood relations is known to them. A positive history of cancer in the family was given by 42 of the 110 ovarian patients (40 per cent), although no women knew the medical history or death causes of any great-grandparents, only 18 knew similarly of one or more grandparents, only 23 knew such facts concerning both parents, and one knew only the cause of death of one parent (cancer of the bowel). It is of interest that the mothers of 15, and

the fathers of eight of the 42 women with a positive family history actually had cancers themselves. Only one patient, a girl of twenty-two, knew of two deaths in the family from cancer. Her father died of cancer of the leg, and his sister, when quite young, died also of cancer.

A study of the duration of the disease from the time of first symptoms showed practically identical survival curves in the group which had a positive history of cancer in the family, and in those which did not.

No other group of pelvic cancers studied in my clinic have given such a high percentage of positive family history, although, of course, 110 cases are far too few to afford any definite data. However, as controls, we have studied the family history of a number of women who had been operated upon for various gynecologic complaints other than cancer. A positive history of cancer in the family was given in 17.3 per cent of 1,045 women under thirty-five, in 25.3 per cent of 1,235 women from thirty-five to seventy-five years, and in 28.6 per cent of 600 women between forty-five and seventy-five years.

The 42 patients gave the following as facts:

Maternal Grandmother: One died each of cancer of the stomach, and of the liver; in a third, the death cause was merely stated as "cancer."

Grandfather: One died of cancer of the stomach and one of the face.

Mother: Five died of cancer of the uterus, three of the breast, two of the ovary, two of the stomach, two of the bowel, and one from what was described only as "abdominal cancer."

Father: Two died of cancer of stomach, two cancer of the "neck," one cancer of the "face," one prostate cancer, one sarcoma of leg, and one cancer of "abdomen."

Aunt: One abdominal cancer, and two described only as death from "cancer."

Uncle: One cancer of the bladder.

Cousin: Cancer of the womb.

Sister: One cancer of the ovary, one each of breast, uterus, stomach, abdomen, and shoulder.

Brother: One cancer of the stomach, one of the tongue, and one of the jaw.

AGE

More than two-thirds of our 110 patients were between the ages of forty and sixty years, yet nearly all age groups were represented in the series. In general, the age curve of the ovarian cancers resembles that found in our 115 cancers of the uterine body. The average age of our women with ovarian cancer is greater than that of either our fibroid patients or those with cervical carcinoma, the age curves of which also resemble each other.

Two of our patients were less than nineteen years. One was a girl of sixteen who died with recurrence four months after removal of a very unusual type of

adenocarcinoma which developed in an ovary which also contained a dermoid cyst. The other patient was nineteen years of age, and had a large papillomatous cyst containing early carcinomatous change. Of interest also is cancer in old women. Ten of our series were between the ages of sixty-five and eighty-one. Five of these died of cancer within three months of their first treatment. One only lived more than nine months: oddly enough, this woman, aged eighty-one, was the oldest in the series, and lived for three and a half years: she had many "tappings." The curve showing distribution of age is shown as Fig. 1.

MENSTRUAL HISTORY

The time when menstruation began is within normal limits. Omitted from this calculation are the 6 granulosa cell tumor cases, and 12 other patients where data are not given.

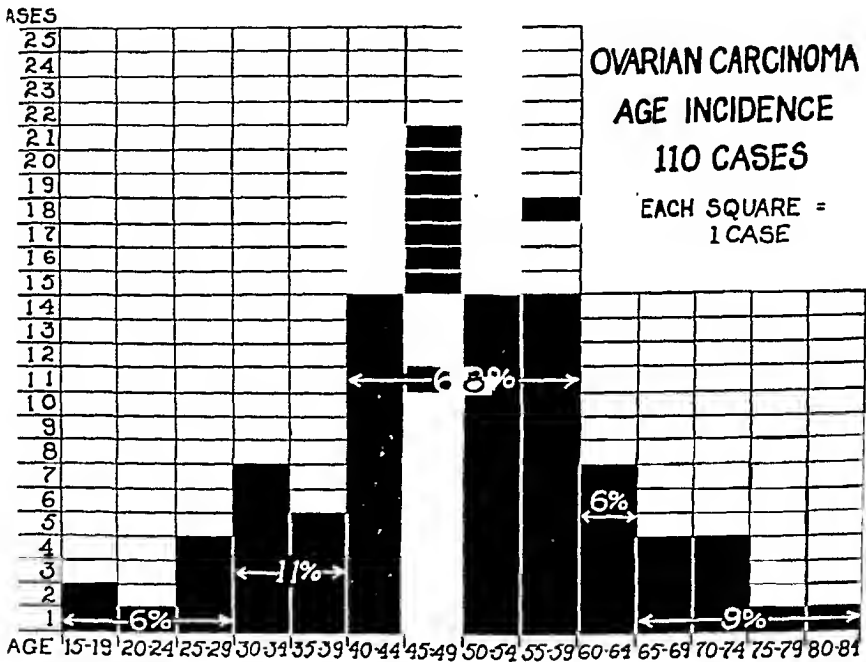


Fig. 1.

Nearly 30 per cent of the 92 patients did not begin to menstruate until fifteen years, or later, and nearly 10 per cent of them not until sixteen, or later. This is normal as is shown by a control study of nine groups, each of 100 gynecologic cases, in which menstruation first began at fifteen years, or later, in 22, 35, 24, 30, 30, 27, 35, 15, and 31 per cent respectively in each group. Another study of 300 women from which fibroids and menorrhagia cases were excluded showed that menstruation began at fifteen, or later, in 30, 30, and 27 per cent respectively in the three groups of 100 each.

TABLE I. ONSET OF MENSTRUATION
92 CASES—AVERAGE AGE 13.9 YEARS

YEARS	CASE	YEARS	CASE
10	1	14	26
11	4	15	13
12	13	16	15
13	18	17	2

When the patients presented for treatment, 40 already had passed through a normal menopause and had had no subsequent bleeding. Seventeen women were menstruating normally and regularly while eight were menstruating irregularly, scantily, or profusely. Two had amenorrhea at thirty-one years of age (one for four years and one for three months). Thirteen were having irregular periods and menopausal upsets, while 12 who had passed through the menopause some years before now had irregular bleeding. The six granulosa cell tumors were excluded also from this section of the compilation, as are twelve cases with incomplete histories.

MARRIAGE AND PREGNANCY

Nearly all series, especially in the older literature, contain a high percentage of unmarried women.

More recently, Byron and Berkoff found 23 per cent of ovarian carcinomas were in single women. Fleming had 20 per cent and McIntyre had 23 per cent in their series. Murphy's figure of 26 per cent more closely approaches the average found in the much older literature.

My own tables give a much lower percentage. Yet it is much greater than the incidence of unmarried women of comparable age in this country (U. S. Census 1920: 9.71 per cent of women over thirty-five years are unmarried; U. S. Census 1930: 9.26 per cent).

All authors report a high incidence of sterility in their series, yet often do not state whether the single women are excluded before the computation.

Cameron, in 1931, stated that 42.8 per cent of his 150 collected cases were nulliparas, and Szathmary, in 1935, found 35.2 per cent, neither author making comment as to whether any were single. Massabuan and Etienne, in 1913, excluded from their computation a number of girls whose ovarian cancers developed before puberty. Of those remaining, 97 had been pregnant, and 26 had not (27 per cent sterility). Strübler and Brandess, 1924, found that 28 per cent of 64 women, whose primary ovarian cancer had developed after the menopause, were sterile, whereas only one of 33 women who had secondary ovarian carcinoma had never been pregnant. Fleming (1931) reported 20 per cent sterility in the married of his series, and McIntyre, 1931, found sterility in 24 per cent of 78 married women with malignant and questionably malignant ovarian tumors. Murphy, 1933, gives sterility in 34.7 per cent of his series. Byron and Berkoff, 1926, found that ten of 44 married patients with ovarian carcinoma were sterile (22.7 per cent).

Strauss, approaching the subject from another angle, notes the small percentage of malignancy in ovarian tumors complicating pregnancy: the low point is one-half of 1 per cent (Siegel) and the high point is 6.6 per cent (Jetter) in such series. It is a fact, however, that the majority of pregnancies are in youth, and not in women of cancer age.

My own tables show a very high incidence of sterility in married women. Excluding the unmarried women from the calculations, I find that 31 per cent of patients had never been pregnant: and that 37.5 per cent had never borne a child—a few had had abortions.

Arranging the figures the other way, I find that only two-thirds of the married women had borne children, but that 42 per cent of the married women had aborted. These figures might challenge the assertion of Blair-Bell, and others, who claimed that parity was of no importance in the etiology of ovarian cancer, especially when we find that Hill, from data obtained from the U. S. Census of 1900, found that only 7.4 per cent of women in Rhode Island, Ohio, and Minnesota, married more than ten years had not been pregnant.

Data concerning abortion are unreliable because abortions often said to be spontaneous actually were induced.

Thirty-seven of my 93 married patients admitted from one to six abortions, 10 women acknowledging from three to six. Thirteen frankly stated that they had had from one to six induced abortions. Only 11 of the 37 women who had abortions subsequently bore a full-term child. Of these 11, 8 bore one child, and 3 bore two.

While too much importance cannot be ascribed to percentages obtained from a small series of cases, it is also true that the literature will never see a series of cancer observed within a single decade large enough to satisfy a statistician as to the accuracy of the deductions, and with sufficient social data to enable the reviewer at least to guess whether the relative sterility was caused by economic conditions, or inability to conceive.

The high incidence of abortion, and the few pregnancies thereafter, suggest that pelvic infection might be of etiologic importance. Yet pelvic infection is common in women of the childbearing age. If it were much of an etiologic factor for ovarian carcinoma, this tumor would be common, whereas it is rare. Two women in my series had ovarian tumors develop shortly after pelvic infection.

FIBROIDS

The rôle constituted by fibroids in sterility is not known. Whether fibroids are causal factors, or merely an occurrence in sterile women is still a question of contention. Nor do we know much more about their frequency in normal women.

We have few statistics on this point other than those of Cullen, who many years ago reported the finding at autopsy of fibroids in 10 per cent of 431 white women more than twenty years of age, and of Young and Williams, who found small fibroids recognizable only when the abdomen was opened at surgery in 2¼ per cent of 1,402 women. Fibroids were present in 20 of my 85 patients (all white) in which we were able to visualize the tumor. Most of them were small and of no clinical importance. Five other women had had operations for fibroids before our treatment. The incidence in the combined cases is 30 per cent. Three of the 20 fibroids might have been of clinical importance had their importance not been overshadowed by a malignant tumor.

FORMER OPERATIONS

Forty-nine of the 110 women had been operated upon several years before admission to my service, exclusive of several others who had had perineal repairs, curettage for incomplete abortions, operations for tonsils and adenoids, hemorrhoids and rectal fissures.

Thirty-five of the 49 had been operated upon many years before the patient could have had the cancer. Nine others had gynecologic operations so shortly before the patient gave evidence of cancer that I cannot be certain cancer was not then present. Five other women, however, were operated upon for stomach, gallbladder, or chronic appendix complaints when the cancer was present but unrecognized, although probably it was causing the symptoms. The fact that somewhere between 34 per cent and 40 per cent of the 110 patients with ovarian cancer had had the need of surgery in the past and unrelated to the present complaint merits attention, especially since I can find no such high incidence of former operative work in 330 gynecologic patients selected as controls. All of this latter group were more than forty years of age and none had tumors. They gave history of but 61 former operations, again excluding perineal repairs, curettage for incomplete abortions, tonsil, adenoid, nasal, and hemorrhoid operations, etc. This is an average of only 20 former operations in each series of 110 controls, the details being 11, 8, and 6 former general surgical operations in the patients with ovarian cancer, and 9, 17, and 10 former gynecologic operations in each group. The figures, however, do not show an unduly high relative proportion of former gynecologic operations, such as I found in patients with fibroid tumors, and which convinced me that a large number of women with fibroids had pelvic tissue that had always been below par. There were 16 former general surgical and 19 former gynecologic operations in the group of 110 ovarian carcinomas; 25 former general surgical and 36 former gynecologic operations in the 330 gynecologic patients over forty and without pelvic tumors, while there were only 71 former general surgical and 210 former gynecologic operations in 683 of my patients with fibroids.

SYMPTOMS AND SIGNS AND DIAGNOSIS

The fearfulness of ovarian cancer is shown by the fact that the disease so often developed insidiously. Sometimes the first symptoms were comparatively trivial, as a vague sense of pressure, or mild gastrointestinal upsets, and yet when the woman came for examination we found that she had an inoperable tumor.

The presence of a tumor was the first sign and only symptom in 6 cases. Two of these patients disregarded our advice and delayed operation until symptoms developed and compelled treatment. The other four did not delay treatment, yet all six had inoperable cancers when they came to surgery. Two only of these six women survived the five-year observation period, and both have recurrences. Dyspnea was the first symptom in several cases, caused by fluid in the chest in two, and abdominal ascites in several others. These also had inoperable tumors. It is startling to find the complacency with which so many of our patients regarded their enlarged abdomens. Some of them only felt that they were getting fat; a few, however, suspected fluid.

With patients coming in because of compelling symptoms, pain was the most common. Usually it was mild at first and not constant, and

then gradually increased in severity. When the pain was epigastric, there was often nausea and vomiting. A few patients came in with abdominal pain so severe that they were certain they had some acute abdominal condition. Sometimes the pain began in the ovarian region and radiated down the thigh, or to the groin or back. Yet the tumor was not always incarcerated in the pelvis when women had these symptoms. Pain, however, did not carry the meaning it does in cervical or uterine cancer, because many women who survived five years after treatment had pain as a symptom. We could not establish a definite relationship between pain and leucocytosis in a study of the cases.

Pain was a complaint in 40 of the 64 women who can be studied for five-year survivals. It was present for three months or less in one-third of the 40, between three and six months in another third, but was "felt off and on" in some form for several years before entry in the other third of cases. The sedimentation time was shortened invariably in the 20 cases in which it is recorded, sometimes being only twenty or thirty minutes.

The menstrual disturbances were variable. Twenty-five of our patients had postmenopausal or menopausal bleeding. When reviewed to see if the bleeding could have been due to fibroids, I find that only two of the 12 postmenopausal bleeding cases had small fibroids, as did two of the 13 women with menopausal bleeding. I did not think these tumors were the cause of the bleeding. Small fibroids were noted also in two women who had irregular menstruation, and in one who had amenorrhea of three months' standing.

Altogether, 316 complaints were given by 106 patients. Their incidence is shown as follows:

TABLE II. SYMPTOMS IN 106 OVARIAN CARCINOMA

Pain	In 70 patients	Bleeding	In 31 patients
Swelling	In 60 patients	Gastrointestinal	In 13 patients
Pressure	In 56 patients		In 6 patients
Tumor	In 39 patients	Amenorrhea	In 2 patients
Loss of weight	In 39 patients		

Physical examination did not always reveal the true character of the lesion when the growth was early, because then the findings were often only those of a pelvic tumor. Most of our errors were made when the woman had a small, fixed, unilateral tumor.

ERRORS IN DIAGNOSIS

The ovarian cancer was sometimes mistaken for fibroids when it was bilateral and the masses were indistinguishable from the uterus and there was no evidence of edema. It was erroneously considered cancer of the rectum in three cases that had rectal bleeding, ribbon stools, and mucous secretion. On the whole, however, the diagnoses

were remarkably correct, probably because there were so many advanced inoperable cases that came in with ascites and a frozen pelvis. One case, however, was missed completely: the patient had much ascites and a small ovarian tumor adherent to a freely movable mass that proved to be carcinomatous infiltration of the omentum.

Three of the six granulosa cell tumors were diagnosed as fibroids, an error easy to make but of no great importance with these tumors which, as a group, are usually relatively benign. None recurred after removal.

Thirteen ovarian adenocarcinomas were diagnosed as fibroids. Two only actually had them, together with an unrecognized ovarian cancer. One knew she had a "fibroid" tumor for seven years and had refused our proposed operation three years before and again upon entry.

We treated the four months' pregnancy size fibroid with radium and did not suspect the accompanying ovarian carcinoma until six months later when the mass was becoming larger instead of smaller. The other patient was treated by immediate operation and the fibroid uterus was removed together with the undiagnosed fist-size cancer. She lives twelve years after operation with a recurrence not yet very troublesome.

In 9 of the 11 remaining cases we erroneously diagnosed hard ovarian cancers as fibroids; 6 of these tumors were unilateral. In none was ascites present as a symptom. Because operation, when conditions are proper, is the routine treatment of fibroids in my clinic, no harm resulted from the error save possibly in two patients. In one we diagnosed a symptomless "fibroid" and proposed operation which was refused. One year later, she returned saying she had had pain for several months. At that time there was no doubt but that she had an extensive cancer. The other woman was under the care of a competent physician for pain that could have no association with the pelvis. A small, hard, symptomless tumor was found on routine examination. The supposed fibroid grew rapidly within three months and caused symptoms. She then came to surgery and was found to have an inoperable cancer.

TREATMENT

Sixty-four patients were treated more than five years ago. Surgery was attempted in all, but in eight in whom there was abundant evidence that their condition was utterly hopeless. All of these died and came to autopsy. Two only of them, however, did not receive some form of ray therapy. The tumor was removed in 26 cases, nearly all with the uterus and opposite ovary as well. Twenty cases were operated incompletely: aiming to take as much tissue as possible with the hope that the roentgen ray therapy would be more effective if the cancer bulk was reduced in size. Ten operations were only exploratory, but afforded a chance of biopsy. Occasionally the tumor was tapped at operation to shrink its size and give better exposure for removal, but only when the case was absolutely inoperable—a spill from a cancerous cyst is never beneficial to the patient.

During the early years of the series, radium was used in 16 cases, sometimes followed by roentgen ray therapy. Four of these had radium preoperatively. In an-

other 4 cases, radium was placed within the tumor itself after a colpotomy. In 4 cases it was left for a short while in the pelvic cavity itself after an incomplete operation. In the other 4 patients, it was inserted into the uterine cavity after an incomplete operation.

Radon seeds frequently were inserted into metastatic nodules at time of operation. We no longer use radium, feeling that far better results can be obtained with the modern roentgen ray. The total dose of radium was never great. One patient received 5,770 mg. hours, the next largest dose was 4,200 mg. hours. I doubt if the radium treatments were of much value.

Roentgen ray therapy had been used almost routinely after operation since 1919, and frequently before it. Until 1925, the machines ran between 120 and 140 K.V. The treatment, however, was usually

FIVE YEAR SURVIVAL CURVE 62 OVARIAN CARCINOMA EXCLUDING GRANULOSA CELLS

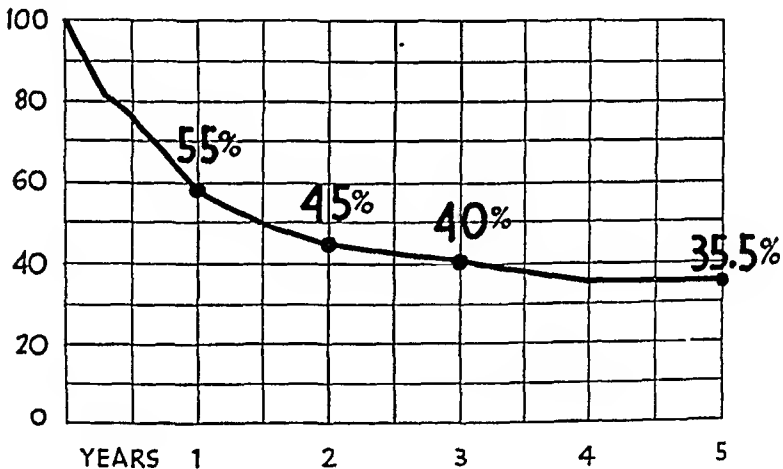


Fig. 2.

incomplete, often being cut short because of x-ray sickness. From 1925 to 1929, nearly all of the patients were treated with 160 K.V. machines, but since 1929, 200 K.V. machines have been used. During these years, ideas concerning roentgen ray treatment have suffered radical changes. Screenage, portals of entry, and the size of the field have been changed almost year by year. X-ray sickness, however, still continues. Only since 1929 has roentgen ray therapy been given in a manner at all comparable to that in which it has been used the past three years.

CURES

By common usage, but not correctly, our 64 cases could be considered for percentages of five-year cures. Yet, we have excluded the two granulosa cell tumors from the computation, because we are primarily

interested in the more malignant ovarian cancers. Properly speaking, five-year cures mean freedom from evidence of recurrence five years after the last treatment, but most of our patients have been radiated several times since then, or even reoperated upon once or twice. Reports in the future, however, will not have this objection. Most of us have learned the dangers of reradiating a patient who has had a full course of treatment with a modern machine. With our large machine, running with one million volts, and the rays screened with 2 mm. of lead, 1 mm. of copper, and 1.5 mm. of aluminum; and the patient's body 17 cm. thick, my colleague, Dr. Robert Stone, has found that 18 per cent of the rays pass completely through a woman's body.

Under the above definition, we have 22 of the 62 patients alive at the end of five years after our first treatment, 35.5 per cent so-called five-year cures. By proper standards, the five-year cures are restricted to patients without evident recurrence five years after the last cancer therapy. Here we have only 11.8 per cent of cases, 11 papillary cystomas with malignant areas, one pseudomucinous adenocarcinoma, and two primary adenocarcinoma. Roentgen therapy supplemented operation in only four of these patients, and radium in four; for details see Tables I, II, and III.

COMMENT

A five-year cure rate of 35 per cent (37 per cent if the granulosa cell cancers are included) seems very gratifying on first sight. Careful scrutiny of my work sheets dispels this thought. First, because many patients have been reoperated or reradiated during a period in which they should not be re-treated but merely observed. Also because some of the slow growing tumors that had been re-treated might have been still present but unrecognized on examination after five years: yet later they might develop and cause death. Second, the cure rate depends largely upon the number of slow growing tumors in the series, important because years may pass before their metastases attack vital organs. For these reasons it is useless to attempt the evaluation of any method of treating ovarian cancer unless the patient has been followed for a minimum of ten years from the date of the last treatment. There are no reports as yet in the literature based on such thought.

We cannot expect to cure the majority of ovarian cancers because the great proportion are inoperable long before they cause symptoms which send them to a physician. "Inoperable" still means what it did before x-ray and radium came into the therapeutic field and when surgery alone offered chance of cure. "Inoperable" then and now means practically incurable even though radium and x-ray have accomplished wonders in a palliative way. Yet inoperable cancers do not invariably kill within five years, no matter what treatment or none has been employed. Numerous reported cases attest this fact. Quite

TABLE I. PAPILLARY CYSTOMA WITH CARCINOMATOUS CHANGE

SURVIVAL YEARS	TUMOR	OPERABLE	REOPERATED	REMOVAL	CYST BROKEN	FLUID	RADIUM	ROENTGEN RAY	FORMER PELVIC OPERATION
<i>Patients Living—Pelvis Free</i>									
18	Single	Yes	No	Complete	No	No	2600 mg. hr.	No	No
17	Single	No	No	Incomplete	Yes	No	No	Yes	No
17	Double	Yes	Yes	Complete	Yes	No	2800 mg. hr.	No	No
13	Double	Yes	No	Complete: cut ureter	Yes	Yes	No	Yes, after 9 months for recurrence	Colpotomy for pus tubes, three years before
12	Double	Yes	No	Complete	Yes	Yes	No	Yes	No
10	Single	Yes	No	Complete	No	Yes	No	No	No
9	Double	Yes	No	Complete	No	No	No	Yes	No
6	Double	Yes	No	Complete	No	No	No	No	No
<i>Died—Suicide: Pelvis Free</i>									
6	Double	Expl. only and 600 mg. hr. ra- dium in tumor	3 years later; BSO supravag. hyster.	Complete 2nd time	No	Yes, first time	600 mg. hr.	No	No

recently Coffey and Humber reported 108 survivors among 991 patients whose cancer (various organs) was adjudged inoperable and hopeless when first seen by them. Only in operable cases may we confidently expect permanent cures, and truly operable cases form a pitifully small percentage of the total series. Operable cases, moreover, can be expected only when the tumor is slow growing and of low malignancy. My series emphasizes this view.

My 22 five-year survivors, some of whom presumably still had non-palpable cancer, comprised 14 women with cancerous areas developing in otherwise benign papillary cystomas, 3 with pseudomucinous tumors and 5 with primary adenocarcinomas.

The 14 papillary cystomas are relict of the 18 such cases of the total series. In all instances the tumor was essentially macroscopically benign although cancer was proved to have been present. The diagnosis, therefore, was microscopic rather than macroscopic, yet 4 of the 18 patients died from cancer before the expiration of the five-year observation period. The 14 survivors fall in four groups. The first consists of 8 women who are living and well and apparently cancer-free. The second consists of one woman, suicide when well for six years. The third consists of 3 patients dead of cancer after the expiration of the five-year observation period, dying six, seven, and eight years respectively after first treated by me. The fourth consists of 2 living with cancer, thirteen and twelve years respectively after my treatment.

In considering the first group, the reader will note from Table I that the cyst was broken at time of operation in 4 of the 8 women who are cited as apparently well and cancer-free. Three of the 4 had roentgen ray therapy. The tumors were removed completely and unbroken in the other 4, only 1 of whom also had treatment with x-ray.

The rôle of roentgen ray therapy in the treatment of these cases merits discussion. Theoretically, papillary cystomas do not react favorably to the rays since the connective tissue cords are surmounted by a single layer of epithelium. Yet the x-ray must have been the curative factor in 2 patients, 1 who survives an incomplete operation after seventeen years; and another who nine months after surgery developed a recurrence that disappeared after radiation, and has not reappeared after thirteen years. Its effect cannot be evaluated in the third patient because the fourth patient also with a cyst ruptured during the removal of the tumor had no roentgen ray and yet survives seventeen years cancer-free. The cure cannot be well ascribed to 2,800 mg. hr. of radium which was given in the vaginal vault after the first operation. A subsequent operation removed a fist-size mass of papillomatous material, none of which has recurred. Surgery for a tumor of low malignancy may properly be credited with the cure.

Roentgen ray therapy cannot be considered of marked curative value in one case in which it was used after the complete removal of the pelvic organs, the patient now living nine years, because two similar tumor patients were treated only by the surgery and lived ten and six years, respectively. The fourth patient in whom the tumor was completely removed unbroken also had 2,600 mg. of radium through a colpotomy wound. It is difficult to conceive that the survival of eighteen years is due to radium rather than the complete removal of a tumor of low malignancy.

The one patient who died from suicide six years after my first treatment is very difficult to understand, because her first operation was exploratory—the cancer did not seem to be one that could be removed completely. Six hundred millicurie hours of radium consequently was given in the body of the tumor through a colpotomy wound. Three years later the tumor was not larger but the woman complained bitterly of vaginal discharge and the fistula. Consequently, I reoperated upon the patient and found to my astonishment that I could remove the tumor practically complete. The growth had not returned three years later (when she died), although the patient had never had roentgen ray. Whether this tumor shrank spontaneously in size cannot be determined. I am certain it was inoperable when first seen. It does not seem likely that 600 mc. hr. of radium could act in such a wonderful manner.

The three women who died of cancer subsequent to the five-year follow-up are of much interest. Two of them may have been survivals due to the slow growing tumors and the surgery rather than to the x-ray. One dead eight years after our surgery may well have had a cancer of the ovary removed two years before admission here, the physician reporting a large ovarian tumor and much fluid as her pathology at that time. The cyst was broken at our operation, consequently was incompletely removed. Subsequently she had several courses of x-ray. The second patient of this group died six years following our surgery, also worthy of note since she also had an ovarian tumor removed and x-ray treatment given two years before her entry here. She was reoperated and again reoperated after my first surgery and each time cancerous material was removed. In the meantime, she had two other courses of x-ray and 5,770 mg. hr. of radium given in the vaginal fornices and culdesac. The third patient was free from recurrence for six years following radical surgery, when the tumor returned and did not react to radium through the vaginal fornix. The fact that papillary cystoma may grow very slowly seems proved by one other patient living thirteen years after operation but with a slow growing metastasis. The cyst was broken during my attempt to remove it, but seemed completely removed. She has received neither radium nor x-ray.

Many urge that roentgen rays cause the disappearance of peritoneal metastases after the primary tumor has been removed fairly completely by surgery. It may so be. Yet it is equally likely that the implants from a cancer of low malignancy disappear spontaneously after the ovary has been removed and its internal secretions stopped. Such phenomena occur in endometriosis after the ovaries have been removed or killed by x-ray. Small metastases on the bladder, or the peritoneal wall of the sigmoid occurred in several surviving cases with papillary cystoma and were treated with the cautery. Until recent years, I ascribed the cure of the metastases to the cauterization of these nodules. Now, however, I feel that they disappeared spontaneously after the removal of the primary tumor. One patient surviving twelve years, but now living with cancer, had such metastases and omental involvement. The omentum was resected. She also had x-ray.

The 3 pseudomucinous tumors also merit attention since in only one was carcinoma noted at the time the primary tumors were removed. The patient survives nine years without evidence of recurrence; she had had neither radium nor x-ray. The 2 other pseudomucinous patients died from cancer thirteen and eleven years respectively after our first operation. The tumors in both cases ruptured before my first operation and pseudomucinous peritonitis followed, necessitating re-operation once repeated again. Cancer presumably appeared a year or two before death and was proved at autopsy. Both women had received much x-ray therapy during their last years without apparent benefit (Table II).

Five of the 39 women with tumors I adjudged to have been carcinomatous from the beginning survived for five years. These more cellular tumors should be more favorable for treatment with the roentgen rays. There is no doubt that the x-ray was responsible for prolonging life in 2 of the 5 cases and possibly a third. In 1 of the 2, the operation was only exploratory since the tumor could not be removed. She had much x-ray in the years that followed, and six years later when the tumor had not increased in size, we explored again. The tumor mass then was not larger, but was still inoperable and the entire abdomen now was fairly studded with metastases. She lived seven years after my first exploratory operation. The second woman had an incomplete operation followed by x-ray. The tumor returned four years later and is still present, although held in check by another full course of the roentgen rays. She lives seven years. X-ray may have been helpful for one patient now living and well for six years. Her cyst was broken when she came to operation: she had much fluid and many metastases in the lower pelvis which I treated with a cautery. I doubt if she will prove a permanent cure. On the other hand, the 2 patients who survived the longest (one fourteen

TABLE II. PSEUDOMUCINOUS CYSTADENOCARCINOMA

SURVIVAL YEARS	TUMOR	OPERABLE	REOPERATED	REMOVAL	CYST BROKEN	FLUID	RADIUM	ROENTGEN RAY	FORMER PELVIC OPERATION
<i>Patients Living—Pelvis Free</i>									
9	Single	Yes	No	Complete	No	No	No	No	No
<i>Died—Carcinoma</i>									
13	Double	No	Yes, twice	No	Before op.	Yes	No	Much	No
11	Double	No	Yes, twice	No	Before op.	Yes	No	Yes	No

TABLE III. PRIMARY CARCINOMAS

SURVIVAL YEARS	TUMOR	OPERABLE	REOPERATED	REMOVAL	CYST BROKEN	FLUID	RADIUM	ROENTGEN RAY	FORMER PELVIC OPERATION
<i>Patients Living—Pelvis Free</i>									
6	Double	No	No	Primary tumors; metast. cauter.	Before	Yes	No	Yes	No
<i>Died, Heart—Pelvis Free</i>									
14	Single	Yes	No	Complete	Yes	No	1327 mg. hr.	No	No
<i>Living—With Carcinoma</i>									
7	Double	No	No	Had metastases	Before	Yes	No	Two times	Ovary resected. Tube and fibroid out 15 yr. before.
<i>Died—Carcinoma</i>									
13	Single	Yes	No	Complete	Yes	No	1160 mg. hr.	No	Vag. hyst. fibroids; one ovary out 6 years before.
7	Double	No; expl. only	Yes; expl.	No	Before	Yes	No	Much	No

years, dying cancer-free from heart disease, and one thirteen years, dying from a recurrence) received no roentgen ray. Small doses of radium, however, were given in both cases, the former 600 mg. hours, and the second 1,160 mc. hr. in the culdesac after the primary tumors were removed. The cases are worth citing at some length.

One woman, who had had a vaginal hysterectomy at forty-four, began to lose weight and strength at fifty years, four months before entry. She had complained of dragging pain on the right side of the abdomen, and groin, intermittently for three months, then almost constantly, keeping her awake at night. It did not change character or position, nor was it modified by meals or the condition of the bowels. The lower abdomen became enlarged a few weeks before entry, whereas it had been flat before. At operation, I found an ovarian cancer 12 cm. in diameter fixed in the pelvis and lower abdomen. It ruptured during removal with discharge of some serous material; some visible particles of the mass could not be removed, and were left on the lateral pelvic wall. Because the operation was not complete, I placed radium in the culdesac and drained through the vagina. The radium dose was only 1,160 mg. hours. The microscopic findings showed a rather wild looking medullary carcinoma which contained cavities filled with hemorrhage and necrotic debris. I felt her condition was hopeless, and as she was not strong enough to stand roentgen ray therapy, I sent her home. From time to time, she wrote me that she was perfectly well, and her abdomen was flat again. Her physician frequently reported negative findings. Twelve and one-half years after this treatment, she returned with a bowel obstruction which caused death. At autopsy, the abdomen was full of cancer of the same type as the primary tumor. Had this woman received roentgen ray therapy after operation, I would have counted her as a five- and even ten-year cure, due entirely to roentgen ray.

The other patient had an enlarged abdomen and pain for three months as a symptom and a unilateral disgerminoma which completely filled her pelvis and was firmly attached by its unbroken capsule to the pelvic wall. The cyst was broken during removal, yet I suppose was rather completely removed. I left 100 mg. of radium in the culdesac for fourteen hours, having made a colpotomy wound. She was desperately sick after the surgery, far too sick to receive roentgen ray. She went home to die, yet returned two years later, practically well. She died fourteen years later from a cardiac lesion without ever giving sign or symptoms that she had ever had a cancer. This case also must be regarded as a cure by fairly radical surgery of a cancer of comparatively low malignancy. Had she had roentgen ray therapy at any time following surgery, I would unhesitatingly credit the cure to the roentgen ray (Table III).

The above review convinces me most firmly that the profession erroneously credits too many cures of ovarian cancer to the roentgen ray. The agent has proved most helpful in a considerable number of advanced cases where the growth rapidly shrank in size and fluid was markedly decreased. Yet at least as many cancers did not respond at all. Moreover, if a patient remains well five or more years after the complete removal of the tumor and subsequent roentgen ray, the important factor in the apparent cure is not as likely to be the radiation as many observers claim. More likely is it to be the complete removal of a cancer of low malignancy. By no means would I restrict the use of the therapeutic roentgen ray as adjuvant to surgery. We should always use it but keep an open mind concerning our results. We will learn facts more certainly and much faster if we follow all our cases through their entire period of survival after our treatment

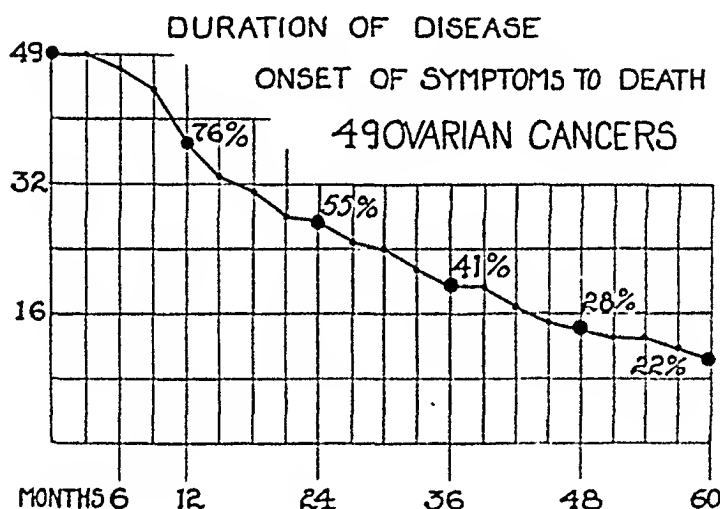


Fig. 3.

before we attempt to evaluate the factors responsible for cure. Only by so doing can we learn the laws that govern the growth of these cancers that now are an unknown factor in determining the frequency of so-called five-year cures.

Tables I, II, and III give the essential data concerning my five-year survivors.

Figures showing the duration of the disease from the onset of symptoms to death in the 49 nonsurvivors show many more slow growing than rapidly growing tumors in my series. Careful study of the microscopic sections gave no support to the theory that the histologic grading of the epithelial cells was of value in determining the radio-sensitivity of the tumor and the prognosis for the patient. The entire known course of the disease after symptoms was less than six months in 2 patients; between nine to twelve months in 9 (24 per cent dead within the first year); between one and two years in 10 (21 per cent),

two and three years in 8 (14 per cent), between three and four years in 6 (13 per cent), between four and five years in 3 (6 per cent). The 11 who were alive five years after the beginning of symptoms (22 per cent) died at various periods, two of them as late as fourteen years after their first symptoms. Most patients surviving five years had intervals free from symptoms when I considered them cured. Two patients now are living but with evident cancer fourteen and thirteen years respectively after their first symptoms. Their cancer has not yet attacked vital structures. The curve as a whole bears a striking resemblance to that of the five-year survivors.

CONCLUSIONS

1. Two-thirds of 110 ovarian carcinomas occurred in women between forty and sixty years of age.
2. Forty per cent of the patients gave a history of cancer in other members of the family.
3. Twelve per cent of the patients had never married.
4. Thirty-one per cent of the married women had never been pregnant.
5. Five-year cures were obtained only when the malignant areas were encapsulated by a cyst wall, or when the tumor was of low malignancy.
6. The value of present therapy cannot be determined with a follow-up of less than ten years' duration, during which period the patient should not be re-treated but should only be observed.
7. The curative effect of roentgen ray therapy in ovarian tumors is much overstated.

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DISCUSSION

DR. DEWITT B. CASLER, BALTIMORE, MD.—Ovarian cancer is insidious in its onset, coming in most cases at a time when women are least conscious of their pelvic condition, beginning usually without bleeding, with pain as the most essential symptom, and inoperable from the time when first seen by the surgeon. The five-year results in ovarian carcinoma are therefore about the poorest of any of our surgical procedures.

The family history of cancer in this series is most interesting to me, 40 per cent having had a positive history in their families. Many of these patients appear to

have a distinct susceptibility to malignancy as I have had three cases of adenocarcinoma of the ovary in which the patient had carcinoma elsewhere. Two cases of adenocarcinoma had also a carcinoma of the breast, and one an associated carcinoma of the sigmoid.

I have long been under the impression that there was a marked disparity in the occurrence of malignant cystadenomas in the white and black races. The last 50 or 60 cases in the Johns Hopkins laboratory showed that the frequency in the whites over the blacks was about 5 to 1. In the granulosa-cell tumors the incidence was about the same for the two races.

It might be interesting to report a Krukenberg tumor that came to me a few years ago. This patient had been operated upon nine months previously for an ulcer of the stomach. Under microscopic examination the ulcer showed a few very peculiar cells which, however, could not be termed definitely malignant. Nine months later this patient came under my observation, and I found Krukenberg tumors of both ovaries and very well-marked carcinoma of the stomach. This gives us a picture of the rapidity of the life history of these tumors.

The results of radium and x-ray treatment of the spindle cell sarcoma are not very satisfactory. In one case where the tumor could be removed except for a very small area in the culdesac, where radium could be placed almost directly on the growth, I assured the family that x-ray should do a great deal but after treatment the tumor spread rapidly. On the other hand, I have just seen a patient who had exactly the same type of spindle cell cystic ovarian tumor, who was operated upon ten years ago and the growth was incompletely removed. That patient has had no x-ray or radium treatment and she is still alive, although she came the other day for a paracentesis.

As far as the treatment of these various ovarian carcinomas are concerned, there seems to be very little difference of opinion about the operative treatment. Since ovarian malignancy is so often bilateral and because it often spreads to the fundus of the uterus, it is generally agreed that complete removal of the pelvic organs and as much of the tumor growth as possible should be done. We have found that most malignant tumors of the ovary respond to x-ray and radium, although the papillomatous cystic carcinomas do not respond so well as the solid, massive type.

There are times when the increase of the growth is restricted in a remarkable way. A colored patient was operated upon by Dr. Cullen six years ago for a very extensive carcinoma of the cystic type which he was unable to remove. No treatment was given after operation because he thought it would not be of help. The patient was readmitted during the next six years 52 times and a total of over 1,000 liters of fluid removed before she finally died of a kidney infection. Autopsy revealed not only a general carcinosis but a generalized tuberculosis of long standing. The pathologists have been extremely interested because in many areas of the abdomen the tuberculous process had strangulated the carcinoma and stopped the growth.

DR. ROBERT A. KIMBROUGH, PHILADELPHIA, PA.—I have briefly summarized a group of 89 cases of ovarian carcinoma from the records of the University of Pennsylvania Hospital.

We have found that histologic grading of these cases is of little or no value in prognosis, and, consequently, we depend entirely upon the gross extent of the disease in predicting the chance of cure.

Group I is comprised of cases in which the whole malignant process was apparently confined to one or both ovaries; 37 per cent of our cases fell into this group. In 38 per cent the primary growth could be removed although some peritoneal implants were left behind (Group II). In the remaining 25 per cent removal of the primary growth was impossible because of widespread metastases (Group III).

The five-year salvage in these groups is as follows: Group I, 85 per cent; Group II, 21 per cent; Group III, 13 per cent. It was interesting to note that 90 per cent of the fatalities occurred within two years following operation.

The value of postoperative x-ray treatment is well exemplified by a small series of cases in which the primary growth was removed but peritoneal metastases were left behind. Five-year salvage was obtained in 43 per cent of this group following postoperative irradiation, while only 13 per cent survived among those who received no x-ray treatment.

DR. WILLIAM P. HEALY, NEW YORK, N. Y.—An important point in the handling of ovarian tumors is that we must not be discouraged by the presence of a large amount of free fluid in the peritoneum or even in the chest cavity. We have had such cases sent to us as incurable but with the removal of the fluid it could be demonstrated that the patient had only bilateral ovarian fibromas.

As to the question of histology and its relation to prognosis, it is interesting that we have had four young women with the embryonal histologic type of cancer of the ovary where a competent surgeon has removed the original tumor and left the other ovary. Usually within a year another large tumor had appeared in the other ovary and the patient was referred for radiation, being considered inoperable. In each instance the tumors have disappeared in from six to eight weeks after irradiation, and the patients have remained well for from six to nine years.

A similar striking case was that of a young woman nineteen years of age, practically carried into the clinic three years ago, with a story of having had a cesarean section a year and a half previously with the removal of a malignant ovarian tumor. She came to the Memorial Hospital frightfully ill, with a large abdomen and multiple tumor masses. The original surgeon reported that the growth had been a very anaplastic type of ovarian cancer. After two months of roentgen therapy we could not find any tumor except deep in the pelvis, and that eventually completely disappeared.

Preoperative roentgen radiation for ovarian cancer is the secret to whatever success you will attain. I have never seen the primary tumor of a papillary adenocarcinoma of the ovary disappear under radiation therapy, but the secondary implants are extremely radiosensitive. In one patient operated upon and regarded as incurable, then treated for two years by tapping and roentgen irradiation at intervals, I have been able ultimately to remove the primary tumor. It is now eight and a half years since I did this in one case.

The worst results are obtained in the patients already operated upon by surgeons who have torn widely into the tumor tissue, opened up lymphatic and blood spaces, but have left a lot of residual cancer. We can only help these patients for a little while with postoperative radiation. I am now teaching that if we believe that a patient probably has a malignant ovarian tumor, and she is beyond the age of forty, radiation treatment should be given and then a delay for several months before operating.

The importance of preoperative radiation is seen in another case. This patient had had amenorrhea for three or four months, and had an enlarged abdomen with palpable tumor masses. Preliminary roentgen irradiation was advised and the abdomen tapped once. No more fluid formed, and six months after coming under my observation we were able to remove the tumor masses and the uterus. There was no evidence of secondaries elsewhere and no more tumor has since formed.

The case with the longest history of tapping that I have ever seen any reference to, was a patient coming with the story of a failure to remove an ovarian tumor seventeen years before and repeated paracentesis ever since. She was a huge woman and when she came to the Memorial Hospital we advised roentgen radiation. Later in spite of the seventeen years of constant tapping we were able to remove all of the tumor tissue. This shows the tremendous resistance of the peritoneum to infection.

DR. CHARLES C. NORRIS, PHILADELPHIA, PA.—I believe ovarian tumors vary markedly in radiosensitivity. I have seen many cases which were extremely radio-resistant. I should like briefly to relate the history of a case which was in some ways extremely susceptible to deep roentgen therapy. This patient, a woman suffering from papillary adenocarcinoma of both ovaries, was operated upon by the late Dr. John G. Clark, a complete operation being performed. No post- or pre-operative irradiation was given. Eighteen months later she was brought to the hospital in an ambulance suffering from a recurrence. The pelvis was "frozen" and in the abdomen a firm, fixed mass rose to two fingerbreadths above the umbilicus. There was considerable ascites and there had been a loss of 20 pounds in weight. The patient had been absolutely bedridden for two weeks. Deep roentgen therapy was instituted and in three months the mass had been reduced to an oval fibrous lesion in the left wall of the pelvis about the size of a pigeon's egg. At six months after the irradiation this mass had increased to the size of an orange or small grapefruit and a small amount of ascites was demonstrable, a second course of deep roentgen therapy again reduced the recurrence to a pigeon's egg in size. During the next six years there were 4 to 5 similar recurrences, each one treated in the same way and with the same result. Histologically the original specimen presented the usual characteristics of a papillary adenocarcinoma. The case is of interest for the following reasons: (a) the speed with which all the recurrences yielded to roentgen therapy; (b) the fact that although the tumor was evidently highly radio-sensitive a cure was not effected despite the many courses of deep roentgen therapy administered; and (c) the fact that no immunity to the rays was developed, the last recurrence yielding as quickly as the first. This patient finally died of a strangulated hernia while out of the city and about seven months after the last recurrence. The case is not recorded as a cure and, as it occurred twenty years ago, did not have the advantage of more recently developed methods of irradiation.

In our series of cases previously reported from the University of Pennsylvania Hospital, we found that the papillary adenocarcinoma (not simple papilloma) yielded about 50 per cent better five-year salvage than the glandular carcinoma and that the secondary carcinomas (i.e. those developing in previously benign neoplasms) gave about twice as good end-results as were secured from those which were malignant from the onset.

We have not found the microscope of great aid in determining radiosensitivity in ovarian tumors. The large variety of malignant neoplasms which develop in this organ greatly hamper careful end-result study. In our study, simple papillomas were classed as semimalignant and were therefore not included in our series.

DR. EMIL NOVAK, BALTIMORE, MD.—It would be valuable if we could discuss separately the end-results of the various types of ovarian cancer. Unfortunately, Dr. Lynch's pessimism is fully justified with most forms of ovarian carcinoma. With others the outlook for the patient is not nearly so bad. This would apply, for example, to many cases of granulosa cell carcinoma, but not to all. A large number of cases of this type have been cured by nonradical operations, such as unilateral salpingo-oophorectomy. On the other hand, we have had cases in our series of over 50 in which even after very radical operations the tumor has returned with amazing rapidity. In one patient, for example, within three months of a very complete operation, the patient returned with a recurrent tumor filling the pelvis and soon proceeded to a fatal termination. Metastases to the long bones have been observed in a few cases in the literature.

On the other hand, the Brenner tumors, while usually classed with the carcinomas, seem to be essentially benign, and I know of only one case in which recurrence is said to have been noted. The dysgerminoma or seminoma, again, is apparently much less malignant than ovarian cancer in general, and in addition is quite radiosensitive.

Krukenberg tumors, being almost always, and according to many always, secondary, offer very little hope to the patient. Although not especially germane to the present discussion, I believe there is good evidence that the Krukenberg tumor may in rare cases be primary in the ovary, and I have observed one or two cases in which this seems to have been the case.

In short, there is no field of clinical gynecology in which pathology is so essential to the proper interpretation of findings and results, and no field of gynecologic pathology which is in greater need of clarification than that of ovarian tumors.

DR. FRED L. ADAIR, CHICAGO, ILL.—We have had the greatest difficulty in knowing what we might expect from either irradiation or operation, and in many cases where we had expected good results we had disastrous ones, and vice versa.

With reference to the particular group of papillary cystomas, we have great difficulty in determining whether these tumors are really malignant. It is obvious that we cannot examine the whole tumor microscopically, and in isolated fields we have difficulty in determining whether a particular field is definitely malignant or not. So I believe we have to accept with more or less skepticism the diagnosis of malignancy in the enormous tumors of this type owing to the impossibility of making a microscopic examination of all portions of the tumor.

One point which must be stressed, in view of the possibilities of irradiation treatment, is the examination of the cellular elements in the fluid, obtained by a paracentesis. It is often possible to make the diagnosis in this way without any exploratory operation. Heretofore we have favored exploratory operation prior to irradiation, but if Healy's opinion is correct, we believe paracentesis for diagnosis with subsequent irradiation and ultimate operation would be preferable.

DR. J. C. LITZENBERG, MINNEAPOLIS, MINN.—We recently analyzed our cases of cancer of the ovary at the Cancer Institute of the University of Minnesota, and our results were so good that I hesitated to report them. But inasmuch as our figures closely parallel those of Dr. Lynch, I have the temerity to say a few words about them. Of our 108 cases nearly 33 per cent were well five years afterward, some of them nine years. This year will have to be completed before we finish the ten-year period.

I also have been impressed with the unreliability of the pathologic diagnosis because of the inherent difficulty of making a satisfactory examination. As an illustration, in one patient the entire peritoneal cavity and intestines were studded with implants that microscopically were diagnosed as cancer. For mechanical reasons the tumor was removed in spite of the apparently hopeless prognosis, and she did not have x-ray treatments. That was eight years ago and she is well at the present time. Five years afterward it was necessary to open the abdomen for another gynecologic condition, and there were none of those implants left. They could not have been malignant, the only treatment having been removal of the cyst.

Our method of treating cancer of the ovary is to remove the cyst and follow our surgery with deep x-ray therapy. Perhaps Dr. Healy's method of preoperative roentgen therapy may be better, but inasmuch as our results are almost parallel with Dr. Lynch's, I thought our figures might be reported here in spite of the fact that we feel that they should be rechecked before publication.

We agree with Dr. Lynch that we should studiously avoid the term five-year cure. We only say five years alive and without recurrence. After ten years perhaps we can say something more definite and reliable about the cases.

DR. LYNCH (closing).—My study has convinced me that x-ray is not the curative agent with ovarian cancers that we have thought it to be. Occasionally it does wonderful things as Healy has described. It sometimes controls fluids but very,

very often fails. When you follow your patients for many years you will come to believe with me that the tumor that is x-ray sensitive is likely to recur. Lymphosarcomas are most sensitive to x-ray, yet x-ray has never cured one of them.

It so happens that we have many patients in our series who were treated with such small doses of radium that the cure must be credited to surgery even though we felt the removal was not perfect. Especially is this true of papillary cystomas, the removal of which is likely to cause recession of peritoneal implants. Papillary cystomas are not sensitive to x-ray yet this is the group of tumors in which we have had the greatest percentage of cures. The tumors which were essentially epithelial are the ones which x-ray should cure, but our results do not force such a conclusion. Possibly these tumors were too widespread, yet several early cases did not react to radium and several others did not recur after complete removal. In the treatment of ovarian carcinoma as in any other malignancy we must be careful in deciding whether the cure was because of the treatment or just happened to follow it. Only by carrying your cases for ten to fifteen years will you know anything as to what your results have been in this blind type of cancer.

ILIAC LYMPHADENECTOMY PLUS RADIATION IN BORDERLINE CANCER OF THE CERVIX*

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(From the Gynecologic Service, Barnard Free Skin and Cancer Hospital, St. Louis)

TWO years ago I described a method of treatment for borderline (Group II) cancer of the cervix, combining radiation of the primary lesion with surgical removal of a large portion of the tributary lymph glands. The first case done in October, 1930, with cancer metastasis in the hypogastric lymph glands is still free of recurrence at the present time, five and one-half years later. In this first report† I separated the cases into Group II and Group III (League of Nations Classification). The patients in Group III had so high a primary mortality that I have not done the operation in these more advanced lesions during the past two years. The total number of patients in Group II operated upon up to the present time is 46.

The experience of the past two years has encouraged me in the belief that by this method of treating borderline cancer of the cervix we have made some little advance, and, Heaven knows, when we are attacking so formidable an enemy as cancer, even a gain of 10 or 15 per cent seems like a victory.

Victor Bonney in his discussion last year agreed to the general principles of this method, even though he could give no definite figures as to the number or results in the cases where he had removed

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25, 1935.

†Iliac Lymphadenectomy with Irradiation in the Treatment of Cancer of the Cervix, *Am. J. Obst. & Gynec.* 28: 650, 1934.

lymph glands alone. It was also of great interest in this connection that 23 per cent of Bonney's patients who had cancer metastasis in lymph glands remained well over five years.

SELECTION OF CASES

Careful selection of cases is a prime requisite to success. First and foremost the patient must be a good operative risk. Heart and kidney disease, obesity, debility or extreme age are contraindications. Just because cancer has a greater tendency to early metastasis in the young, I have applied this method wherever possible to younger individuals. The average age of the 46 patients subjected to lymphadenectomy was forty-one years, compared to forty-six and one-half years for the entire group of cervical cancer patients treated during this period of time. Fifteen patients were thirty-five years of age or less, and five were between twenty-two and twenty-nine years of age.

MORTALITY

There have been two deaths among the 46 patients operated upon up to the present time, a primary mortality of 4.3 per cent. An analysis of these two deaths shows that the concomitant radiation was an important, if not the main, cause of the fatality. One patient died eight days after operation of embolism probably due to a gold radon seed implanted close to the uterine vessels. The second death occurred on the sixth day after operation from peritonitis. At autopsy it was shown that the radium capsule placed in the cavity of a bicornuate uterus, whose rudimentary horn had been removed, caused a slough and perforation into the broad ligament, with infection spreading thence to the abdominal cavity. These two deaths have induced me to avoid all radiation treatment at the time of operation. Whether my abandonment of intraabdominal radiation is a wise step cannot yet be predicted. Possibly deep x-ray will accomplish as much as radon seeds in the destruction of cancer cells that have not reached the lymph glands. At any rate I believe it is imperative that every risk to the operation be eliminated, so that the mortality will be not appreciably greater than the 0.5 per cent attendant upon radiation. Technically the difficulties are not great. I have thus far caused no injury to the large vessels, although the dissection of the lymph glands approximates them closely. We must know when to stop. If the gland is broadly adherent to the vein, it is wiser to desist. In two patients included in this series one such adherent lymph gland was left, although the remainder were removed. In three other cases an exploratory operation showed the lymph gland mass so large and adherent that the operation had to be abandoned. Two of these received intraglandular radiation. There was no mortality in these three cases, but they were of course not included in the present series.

Postoperative complications were infrequent. One patient developed a broad ligament hematoma with subsequent infection that had to be drained from above.

TECHNIC

Naturally the technic of a new operation of this kind will be modified by experience. I have already touched upon the separation of operative measures from radiation treatment. Recently where heavy radiation preceded the operation, I found that the lymph glands were more likely to be adherent and difficult to remove. Hence I would advise the following procedure: Approximately 1,000 to 1,500 r. units of deep x-ray therapy spread over two weeks. Two weeks after this series is concluded iliac lymphadenectomy is done. Two weeks after operation an intrauterine application of 150 mg. radium in gold capsules totalling about 4,000 to 5,000 mg. hours is made. An additional 2,000 to 2,500 r. units of deep x-ray should follow the radium treatment.

Spinal anesthesia which was preferred in the first series, has become routine in the past two years. As a rule 200 mg. of novocaine dissolved in the spinal fluid has been injected. The intestinal relaxation following spinal anesthesia is essential to proper inspection of the pelvic cavity. In cases where ether had to be used to supplement the spinal anesthesia, it was found advantageous to use inhalation of about 25 c.c. of vinethene as an intermediary. This method avoided the struggling that previously was encountered at the beginning of the ether narcosis.

In the operative technic the most important change in the past year has been the additional removal of the glands situated over the external iliac vessels near their exit from the abdominal cavity. These glands are usually enlarged and their removal is relatively easy. How often they are involved in cervical cancer remains to be seen. Cameron Duncan who recently reported a small series of iliac lymphadenectomies suggests routine ligation of the uterine arteries. I cannot agree that this will be without considerable added risk in many cases. Where a ureteral gland must be removed, such a ligation may be necessary but anything that complicates or unduly prolongs the operation must be avoided. The routine removal of all loose fat in the area exposed, as suggested by Duncan, has been done by me in all cases for several years. Abdominal implantation of gold radon seeds has been abandoned for two years as not devoid of dangers and probably not more effective in the destruction of connective tissue extension than a full course of x-ray therapy. The operation requires about one to one and one-half hours for completion.

GLAND METASTASIS

Glandular metastasis in these 46 cases was found 15 times (33 per cent). This is considerably lower than I reported in my first series (44 per cent). The change is evidently due to the fact that almost all patients in the past two years have been subjected to heavy previous radiation treatment. A division of patients receiving little or no radiation and those receiving heavy radiation before operation showed that in 20 unirradiated patients, cancer was found 9 times (45 per cent) whereas in 26 preradiated patients, lymph gland metastasis could be diagnosed in only six (23 per cent). From analogy with radiated lymph gland metastasis elsewhere I cannot believe that all



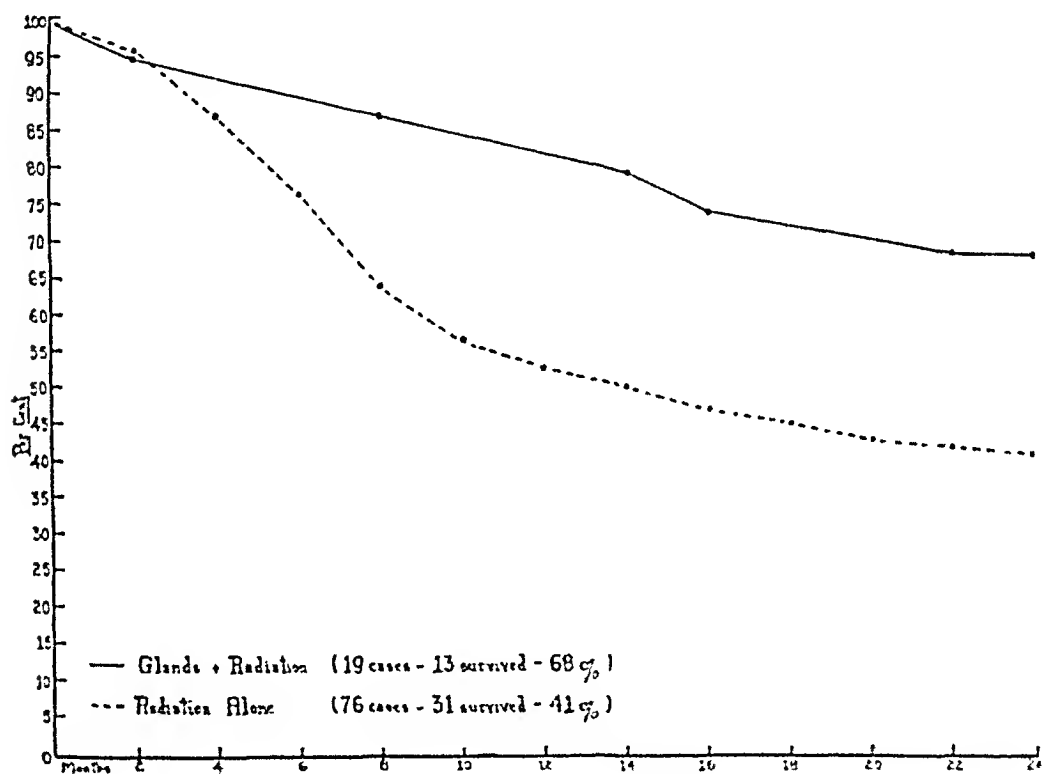
Fig. 1.—Iliac lymph gland, containing a small nest of epithelial cells showing degenerative changes and calcium deposits, that suggest a radiated cancer metastasis.

cancer cells have been destroyed by this preliminary radiation but merely that their recognition has been made more difficult. Occasionally we found areas, as seen in Fig. 1, that strongly suggest an irradiated cancer nest.

A total of 194 glands were removed in these 46 patients and subjected to careful microscopic study. Many unusual conditions were encountered that will be the subject of a later publication. Unfortunately we know too little of the normal and pathologic anatomy of lymph glands. The question whether there was any marked tendency to glandular metastasis in the more anaplastic tumors must be answered in the negative. Out of 43 cases on which data were available the cervical lesion in seventeen was classified as Grade 1 or 2 and showed 5 gland metastases (29.4 per cent) whereas in 26 the cervical

cancer was classified as Grade 3 or 4, and showed 9 metastases (34.6 per cent). One additional case in the former group would have evened the difference.

And now to come to the crux of the problem. What was the survival rate of patients treated by this method and how does it compare with the survival rate of patients of the same group treated in the same institution by radiation alone? Since only two patients had been operated upon more than five years ago, I had to content myself with an analysis of two-year and four-year survivals. I realize that even here we are dealing with small numbers, and it would be dangerous

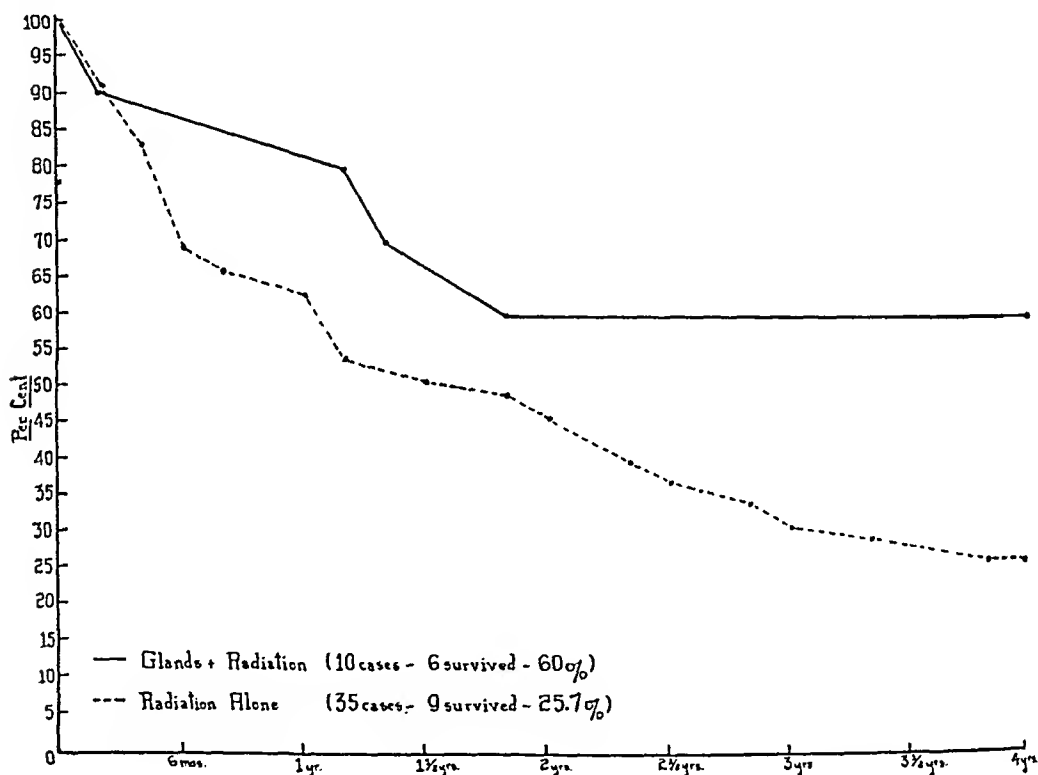


Graph 1.—Two-year survival curve.

to draw any positive conclusions. Nevertheless the difference in results obtained is so striking that I feel encouraged in continuing this plan of treatment and recommending it for trial by others. In Graph 1 the 19 patients operated upon two years or more ago are compared with 76 patients treated with a similar dose of radiation but without lymph gland removal in our hospital during this same period of time (October, 1930 to April, 1934). Except for the first drop due to operative mortality, the survival curve remains definitely higher in the group of lymphadenectomies. In Graph 2 we see the survival curves of patients treated over four years ago, ten lymphadenectomies with radiation, compared with 35 patients whose cancer showed the same stage of involvement not operated upon but radiated by the same

method during the same period of time (October, 1930 to April, 1932). The percentage of survival in the operated cases was found to be approximately twice as great as those receiving radiation alone.

Unfortunately any new method of treating cancer must combine a large experience over a long period of time before drawing even tentative conclusions. If the favorable results thus far obtained in the treatment of borderline cancer of the cervix will encourage others to give this operation a trial, we may before long have an answer to our problem. My experience of the past five years has convinced me that iliac lymphadenectomy in the hands of a competent surgeon, done upon patients that are good operative risks with only partial cancerous



Graph 2.—Four-year survival curve.

involvement of the broad ligaments, is a relatively simple and harmless procedure and gives an increased chance of survival and cure that definitely justifies this surgical intervention.

3720 WASHINGTON AVENUE

DISCUSSION

DR. WILLIAM P. HEALY, New York, N. Y.—Naturally Dr. Taussig has had to choose favorable cases, favorable for surgical intervention. That may make a little difference in the small series, in end-results. Our clinical grouping, in cancer of the cervix, into early, borderline, advanced, and palliative cases, is a very unsatisfactory classification, because so-called early cases have died within the first year, indicating they could not have been early, and cases that have been labeled palliative have gone into a five-year cure group. We are handicapped by the fact

that about 40 per cent to 45 per cent of the apparently favorable cases, according to Bonney's experience, have parametrial lymph gland involvement. That explains the figures for the end-results we get with treatment by radium and x-ray. Most of the cases with a small cervical lesion will give about 80 per cent of five-year cures, but the less favorable cases will drop the results down so that we average in early cases about 55 per cent to 65 per cent five-year cures, which corresponds to the percentage of cases without lymph gland involvement.

Only one in three of Dr. Taussig's cases had gland involvement and they were therefore relatively early and favorable cases for cure. With radiation alone he could get a fair percentage of cures.

I had the privilege of seeing Dr. Taussig operate some years ago upon a patient who had not as yet been irradiated, which I thought was very unfortunate. Dr. Taussig now suggests, and I think rightly, that before any surgical procedure is carried out the patient should have preliminary deep x-ray therapy up to, we will say, 1,500 roentgen in each field, I hope in six fields, two anterior, two posterior, and two lateral. And then in six weeks he will do the operation and two weeks later apply radium. I still think it is a mistake to do the operation before radium has been applied and before the primary lesion has been completely destroyed by radiation.

Four months after radiation with roentgen ray and radium is completed a supra-cervical hysterectomy may be performed without disturbing the cervical field at all, but with the cleaning out of both broad ligaments. It will be a relatively simple procedure, and you will have done it at a time when probably there is complete quiescence in the lymphatic field as far as active cancer cells are concerned. Nevertheless you will have violated a very important rule of radiation therapy because you will have destroyed lymphatics that have become fibrosed by radiation. While you will undoubtedly take out some cancer, you will, on the other hand, have opened up fibrosed areas on the borders of your incision which would have probably kept the cancer locked up indefinitely. I think you will not, in the final analysis, add anything to the total salvage by any modified surgical procedure or by anything short of a Wertheim operation preceded by irradiation.

I have a specimen taken from a borderline case of carcinoma of the cervix, a young woman forty-one years of age, treated by deep x-ray therapy, 2,400 roentgens to each of four fields, followed by radium. For fifteen months she was free from any evidence of disease, and then on the rectovaginal septum there was found a local recurrence which responded to radiation with radium. The pelvis at no time showed any evidence of recurrent disease, but last December, which was about twenty-two months following her primary treatment, the patient began to have backaches and pains in her legs, and about ten days ago she developed complete anuria. The only thing that we had been able to find between last December and the time of her death was an impression of gland masses along the spine, on each side of the lower abdomen. When she came into the hospital with complete urinary suppression, ureteral catheters were passed and 80 ounces of urine was obtained in twenty-four hours, and then the ureters closed down again completely. There were solid cancer masses on each side of the spine and in the retroperitoneal glands, huge kidneys, and a very sharp angulation in the ureter on the left side from that gland mass. The pelvic fields had been completely taken care of by radiation, and there was no evidence of disease in the uterus or pelvis at the postmortem. I think there is little question that our present methods of irradiation and our ability to take care of these peritoneal lymphatics are becoming more and more satisfactory without going on to surgery.

DR. FRANK W. LYNCH, SAN FRANCISCO, CALIF.—Dr. Taussig is helping us learn the frequency of involved glands concerning which we know little. The observations of Schauta many years ago merely showed that glands were rather frequently in-

volved in the autopsy material he was studying. Kundrat, Kermauner, and Sampson subsequently worked in this field. Aside from these, no one has done much of importance except Comyns Berkeley and Victor Bonney.

Dr. Taussig's resection of glands may prove of value therapeutically. The method is well worth trying, since we are curing about as many cases with radium and x-ray as we are ever likely to do. The longer I follow my cases, the less enthusiastic I am over the treatment of early cervical cancers with radium or x-ray alone. Recently a patient with a very early case died from recurrence seven and a half years after treatment. She had one of the earliest microscopic lesions I have ever seen and was radiated by methods which are proper at the present time. Another patient with a very early lesion died from a heart complication five years after treatment, and at autopsy we found involved glands which had not been recognized clinically. Last year we had two Group III cases of patients well for twelve years, develop recurrences and die thirteen years after treatment.

Unfortunately I have only performed Dr. Taussig's operation five times, all on Group III (A.C.S.) cases. The glands were involved only in two. My follow-up which is complete from treatment to death or survival for nineteen years is teaching me that about all you can expect in treating inoperable cancers is to prolong the life of the patient. If you follow the patients long enough, you will find that they will tend to die from cancer.

The case that Dr. Healy has just reviewed is one of the many new forms of cervical cancer that we have seen since using radium. With radium we tend to cure the local lesion and allow the cancer to grow in places in which we never before have seen it. I have seen fluid in the abdomen and masses in the mesentery that you would be certain were ovarian, yet autopsy proved were cancer that had come from the cervix. I feel that when glands are removed around early lesions that we will not be likely to see cases like this one who died with cancer of the kidney.

DR. TAUSSIG (closing).—In the treatment of cervical cancer we should employ to some extent a comparison with other forms of carcinoma. Take cancer of the breast for instance. Radiation attack on the lymph glands, although in the axilla they lie right under the skin, has failed absolutely. I do not know what happens when cancer gets into the lymph glands, but in some way it becomes more resistant to radiation treatment. When simple mastectomy was done for cancer of the breast, the cures were pitifully rare. Then the radical removal of the lymph glands was begun and although cancer was found only in a limited number of those lymph glands, the percentage of cures was markedly increased. If in only 33 per cent cancer was found, this does not mean that cancer was not present in a very considerable number of the remaining cases.

I feel, therefore, that any surgical lymph gland removal that will supplement radiation without an accompanying high mortality is a justifiable one.

Hamant and Durand: *Hysteroscopy*, *Rev. franç. de gynéc. et d'obst.* 31: 1, 1936.

In the opinion of the authors, hysteroscopy now has a definite technic which makes it of practical use. It has no dangers and it is very easy to employ. It is the most certain way to make a diagnosis of intrauterine abnormalities because of direct vision and the possibility of a biopsy. In a short space of time perfected instruments will enable us to employ catheterization of the fallopian tubes. The authors believe hysteroscopy will prove as useful as cystoscopy.

J. P. GREENHILL.

PREMATURE RUPTURE OF THE MEMBRANES AS A MEANS OF INDUCING LABOR*

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(From the Department of Obstetrics and Gynecology, Iowa State University)

DURING the past three years, rupture of the membranes has been employed to complement medical induction of labor with castor oil and quinine, with or without pituitary extract. In the majority of instances there was no medical indication for the induction, which was used as a convenience procedure in an attempt to reduce the period of hospitalization for waiting patients. Only two contraindications, contracted pelvis and abnormal presentation, were recognized. Six hundred and eighty-one records have been studied and form the basis for this communication.

General Data—Parity.—There were 195 primigravidas and 486 multigravidas. In the early period of the work, there was a tendency to limit the procedure to parous women, but more recently it has been recognized that the primiparous cervix rarely offers any real difficulty to instrumental rupture of the bag of waters.

Type of Pelvis.—The pelvis was normal except in 10 patients, who had insignificant degrees of contraction (funnel pelvis 10, simple flat 1, generally contracted 1, and obliquely contracted pelvis of unilateral lameness 1).

Presentation.—There were 672 cephalic and 9 breech presentations, although generally the latter were excluded through fear of prolapse of the cord. Among the former, the occiput was to the left in 384 (57 per cent) and to the right in 288 instances.

Height of Presenting Part.—The presenting part was floating in 335 cases and was fixed but still above the spines in 300 others, leaving only 46 patients with the head actually engaged.

TABLE I. HEIGHT OF PRESENTING PART WHEN MEMBRANES WERE RUPTURED

Floating	322
Fixed—above spines	300
Engaged—at spines	39
Engaged—below spines	7
No data	13
	681

Condition of the Cervix.—The cervix was completely effaced in only 6 instances, but was thinned to some extent in 42 others, while it was thick and uneffaced in 633. The canal admitted one finger in 468 cases and two fingers in 181 cases, while in 32 instances it was closed necessitating digital or instrumental dilatation before the amnion could be reached.

Complications of Pregnancy.—The pregnancy was normal in 597 instances, while in the remaining 84, there were various complications some of which offered indica-

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Abbecon, N. J., May 25 to 27, 1926.

tions for the interruption of the pregnancy (eclampsia 1, nonconvulsive toxemia of late pregnancy 45, cardiovascular disease 4, and pyelitis 7) while the remainder were more or less incidental.

Analgesics Employed.—The usual clinic criteria for the administration of analgesics were followed: in 469 cases none was given, but the remaining 212 patients received some sedative drug (morphine and scopolamine 127, morphine 33, barbituric acid preparations 51, and rectal ether and oil 1).

Anesthesia.—Except in 28 instances when the rapidity of delivery made it impossible, anesthesia was employed as usual (ethylene 579, ethylene and ether 25, open ether 38, chloroform 3, local infiltration 7, and spinal 1).

Preliminary and Subsequent Oxytocic Medication.—In only 7 cases was rupture of the membranes employed without preliminary medication given to induce labor. In 333 instances, castor oil and quinine were given alone while in 336 several small doses (2 to 7 minims) of pituitary extract were also administered (usually by hypodermic injection). Quinine was used alone in 5 patients. In 182 instances, painful uterine contractions had begun before the membranes were ruptured and labor would probably have continued even if nothing more had been done.

In 323 cases no medication was given after the membranes were ruptured, but if painful uterine contractions did not appear promptly small doses of pituitary extract were employed. When the latent period was longer than twenty-four hours, the regular medical induction was repeated. In one case where early delivery seemed imperative a Voorhees' bag was introduced.

Technic of Rupture.—The actual technic for rupturing the membranes varied somewhat with different individuals but in general was most easily accomplished with Allis clamps, provided with special long curved handles (overall length 24 cm.) which had been made up especially for this purpose. Vaginal examination was carried out under sterile precautions, and after the bag of waters was punctured, careful exploration was carried out to determine that the cord or an extremity had not prolapsed. Mercurochrome (2 per cent) was poured into the vagina at the conclusion of the manipulation. Patients were not permitted out of bed unless the presenting part was firmly engaged.

Results—Direct.—In only a few instances was there any unfavorable development directly related to the release of the amniotic fluid. There were five prolapsed cords, a higher incidence than should have been noted if spontaneous rupture of the membranes had been permitted; two of these babies were lost and their deaths may be attributed to the procedure. Prolapse of an arm occurred once and demanded later intervention to accomplish delivery. Moderately profuse bleeding occurred once on the basis of a marginal placenta previa, but might have been expected in any event when uterine contractions lengthened the lower segment.

MATERNAL RESULTS

Latent Period.—The period from the rupture of the membranes to the appearance of definite labor pains was less than one hour in 398 patients. Excluding the 183 individuals who were probably in early labor following medical inductions, there were 215 who responded almost immediately to the procedure. On the other hand, the latent period was longer than twenty-four hours in 32 cases (4.7 per cent) with the longest interval eighty-eight hours. In one case, where early delivery seemed imperative, a Voorhees' bag was introduced to stimulate painful contractions.

Prolongation of the latent period beyond twenty-four hours was noted most frequently in those women who had had three or more children, whereas very short latent periods (less than one hour) were less common in primigravidas who nevertheless usually (97 per cent) went into labor in less than twenty-four hours.

TABLE II. THE LATENT PERIOD

	NO.	PER CENT
Less than 1 hour	398	58.4
1 to 6 hours	208	30.5
6 to 24 hours	43	6.3
More than 24 hours	32	4.7
	681	99.9

TABLE III. LATENT PERIOD IN RELATION TO PARITY

NUMBER OF PREVIOUS CHILDREN	LATENT PERIOD									
	TOTALS		LESS THAN 1 HOUR		1 TO 6 HOURS		6 TO 24 HOURS		MORE THAN 24 HOURS	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
None	195	29	101	52	68	35	19	10	7	3
One	146	21	96	66	41	28	6	4	3	2
Two	109	16	69	63	33	30	3	3	4	4
Three to five	155	23	94	61	44	28	5	3	12	8
Six and more	76	11	38	50	22	30	10	13	6	8
Totals	681	100	398	59	208	30	43	6	32	5

Duration of Labor.—Labor was rapid (under six hours) in 56 primiparas (28.7 per cent) and in 297 multiparas (61.1 per cent), and lasted more than thirty hours in 8 primiparas (4.1 per cent) and in 5 multiparas (1.0 per cent). The distribution according to parity is shown in Table IV.

TABLE IV. DURATION OF LABOR IN RELATION TO PARITY

PREVIOUS CHILDREN	TOTAL IN GROUP	0-3 HOURS		3-6 HOURS		6-12 HOURS		12-18 HOURS		18-30 HOURS		MORE THAN 30 HOURS	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
None	195	11	5.6	45	23.1	66	33.8	47	24.1	18	9.2	8	4.1
One	146	31	21.2	61	41.8	41	28.1	11	7.5	2	1.4	0	0.0
Two	109	16	14.7	47	43.1	31	28.4	8	7.4	5	4.6	2	1.8
Three to five	155	39	25.2	55	35.5	43	27.7	12	7.7	4	2.6	2	1.3
Six and more	76	22	28.9	26	34.2	20	26.3	5	6.6	2	2.6	1	1.3
Totals	681	119	17.5	234	34.4	201	29.5	83	12.2	31	4.6	13	1.9

No directly comparative figures are available, but it is obvious that when labor is completed within twelve hours by 62.5 per cent of primiparas and within six hours by 61.1 per cent of the multiparas, the average birth process cannot be considered prolonged.

Method of Delivery.—Parturition was spontaneous in 642 instances (94.3 per cent) even though the usual indications for operative intervention were observed, and several low forceps extractions were done because of complicating maternal disease. Among the primiparas, the operative incidence was 10.8 per cent and in the parous group 3.7 per cent.

Blood Loss.—The average blood loss was 227 c.c., but there were 21 patients (3.1 per cent) who suffered more or less severe postpartum hemorrhages (more than 600 c.c. blood loss). When the latent period was longer than six hours, the incidence of postpartum hemorrhage was considerably increased, but prolongation of labor had the most significant effect.

TABLE V. BLOOD LOSS IN RELATION TO LATENT PERIOD

LATENT PERIOD	BLOOD LOSS					
	TOTAL IN GROUP	LESS THAN 200 C.C.		200 TO 600 C.C.		MORE THAN 600 C.C.
		NO.	%	NO.	%	NO. %
Less than 1 hour	398	202	50.8	185	46.5	11 2.8
1 to 6 hours	208	103	49.5	99	47.6	6 2.9
6 to 24 hours	43	20	46.5	21	48.8	2 4.7
More than 24 hours	32	17	53.1	13	40.6	2 6.3
Totals	681	342	50.2	318	46.7	21 3.1

TABLE VI. BLOOD LOSS IN RELATION TO LENGTH OF LABOR

DURATION OF LABOR	TOTAL IN GROUP	BLOOD LOSS					
		LESS THAN 200 C.C.		200 TO 600 C.C.		MORE THAN 600 C.C.	
		NO.	%	NO.	%	NO.	%
Less than 6 hours	354	191	53.9	155	43.8	8	2.3
6 to 18 hours	283	133	47.0	141	50.0	9	3.2
More than 18 hours	44	18	40.9	22	50.0	4	9.1
Totals	681	342	50.2	318	46.7	21	3.1

Puerperal Morbidity.—There were no maternal deaths in the series. The total morbidity rate, based upon a reading of 100.4° F. at any time during the first ten days of the puerperium with temperatures taken every four hours day and night, was 24.1 per cent. In 102 of the 164 febrile patients, the temperature elevation subsided in less than twenty-four hours, leaving a more-than-one-day fever incidence of 9.1 per cent. In only 7 instances (1.0 per cent) did the fever persist for more than one week. There were 17 patients (2.5 per cent) in whom the fever was ascribed to extrapelvic conditions; it is our policy to attribute all febrile reactions to pelvic infection unless there is satisfactory clinical evidence to the contrary, even though there may be no signs of pelvic involvement. It is evident from Table VII that, primiparity and prolongation of the latent period and of the length of labor are definite factors in the production of febrile reactions. Other statistics from the clinic, although not strictly comparable, suggest that the incidence of mild uterine infection is slightly higher in this series, probably by reason of the fact that each patient was subjected to at least one vaginal examination.

TABLE VII. POSTPARTUM FEVER IN RELATION TO VARIOUS FACTORS

HIGHEST POSTPARTUM TEMPERATURE	PREVIOUS CHILDREN		LATENT PERIOD				DURATION OF LABOR	
	NONE	1 OR MORE	UP TO 6 HOURS		MORE THAN 6 HOURS		UP TO 12 HOURS	
			NO.	%	NO.	%	NO.	%
Under 100.4° (517 cases)	133 68.2	384 77.0	463 76.4	54 72.0	430 77.6	87 68.5		
100.4° or more (164 cases)	62 31.8	102 23.0	143 23.6	21 28.0	124 22.4	40 31.5		
Totals	195	486	606	75	554	127		

Fetal Results.—There were 29 premature babies (under 2,500 gm.) mostly from patients who presented medical indications for intervention, and 53 children of over 4,000 gm., the largest of which weighed 5,200 gm. The average birth weight was 3,320 gm. There were 11 stillbirths (1.62 per cent) and 10 neonatal deaths (1.47

per cent) with 9 of the fatalities occurring among the 29 premature infants. Among the 652 children, weighing more than 2,500 gm., there were 12 fatalities (1.8 per cent). The assigned causes of death in the two groups, based largely on autopsy findings, are shown in Table VIII.

TABLE VIII. ASSIGNED CAUSES OF STILLBIRTHS AND NEONATAL DEATHS

BIRTH WEIGHTS (GM.)	CAUSES OF STILLBIRTHS					CAUSES OF NEONATAL DEATHS				
	MATERNAL TOXEMIA	HYDROCEPHALUS	INTRACRANIAL HEMORRHAGE	PROLAPSE OF CORD	PREMATURITY	PREMATURITY	INTRACRANIAL HEMORRHAGE	CONGENITAL MALFORMATIONS	ATELECTASIS	HEMORRHAGIC PNEUMONIA
Up to 2,499 (29 cases)	2	1	1	1	1	0	1	1	0	0
2,500 to 3,999 (599 cases)	2	0	2	1	0	1	3	1	1	1
4,000 and more (53 cases)	0	0	0	0	0	0	0	1	0	0
Totals	4	1	3	2	1	1	4	3	1	1

Intracranial hemorrhage, with 7 deaths, heads the list, with congenital malformations, maternal toxemia, and prematurity occupying their usual dominant positions. Only the two fetal deaths ascribed to prolapsed cord can reasonably be charged against the method of induction of labor and such accidents occur even when the membranes rupture spontaneously. One funic prolapse occurred in a patient with a breech presentation. Study of the method of delivery in the cases which resulted in loss of the baby emphasized again the risk of breech extraction, where the uncorrected mortality was 5, or 56 per cent. One other baby died during a midforceps extraction, while in the remaining 15 deaths the deliveries were spontaneous.

TABLE IX. STILLBIRTHS AND NEONATAL DEATHS IN RELATION TO LATENT PERIOD

LATENT PERIOD	TOTAL IN GROUP	STILLBIRTHS		NEONATAL DEATHS		TOTAL DEATHS	
		NO.	%	NO.	%	NO.	%
Less than 1 hour	398	3	0.75	8	2.01	11	2.76
1 to 6 hours	208	4	1.92	1	0.48	5	2.40
6 to 24 hours	43	3	7.00	0	0.00	3	7.00
More than 24 hours	32	1	3.13	1	3.13	2	6.26
Totals	681	11	1.62	10	1.47	21	3.09

TABLE X. STILLBIRTHS AND NEONATAL DEATHS IN RELATION TO LENGTH OF LABOR

DURATION OF LABOR	TOTAL IN GROUP	STILLBIRTHS		NEONATAL DEATHS		TOTAL DEATHS	
		NO.	%	NO.	%	NO.	%
Less than 6 hours	354	5	1.41	5	1.41	10	2.82
6 to 18 hours	283	5	1.77	4	1.41	9	3.18
More than 18 hours	44	1	2.27	1	2.27	2	4.54
Totals	681	11	1.62	10	1.47	21	3.09

Prolongation of the latent period definitely increased the risk to the infant (Table IX) with intracranial hemorrhage accounting for three of the 5 fatalities, although in two instances the labor was completed in less than six hours.

In general, the fetal and infant mortality increased as the duration of labor was prolonged.

Among the primiparas, the fetal loss was 4.1 per cent, and among the parous patients, 2.2 per cent. In the former group, maternal toxemia and intraeranian hemorrhage led the causes of death.

DISCUSSION

This considerable experience with the induction of labor by rupture of the membranes combined with the administration of the commonly employed oxytocic agents has led to the belief that it is more effective and less harmful than other recognized mechanical procedures previously recommended for the same purpose. Its simplicity is indicated by the fact that some dozens of internes with little experience carried out the prescribed technic in the large majority of these cases without serious accident to the mother, and with no more than two infant fatalities that could be attributed to the procedure. In 95 per cent of this series, labor was inaugurated within twenty-four hours after the membranes were ruptured, and was completed in no longer than the anticipated time. In spite of the fact that the presenting part was unengaged in 335 instances, there were only 5 prolapsed cords.

Deliberate rupture of the bag of waters prematurely has made it necessary to change our conceptions of the difficulties of "dry labor," which were formerly stressed and to conclude that dystocia under such circumstances must be due to some other factor such as uterine inertia, faulty mechanism, or abnormality of the bony pelvis. Moreover, it has been necessary to revise our ideas of the mechanism of cervical dilatation by minimizing the effect of the "dilating hydrostatic wedge" principle and emphasizing rather the pulling up of the lower segment by the shortening uterine body and the contractions of the longitudinal fibers of the isthmus and cervix.

CONCLUSIONS

The induction of labor by premature rupture of the membranes after stimulation of the uterus through the action of castor oil, quinine, and pituitary extract is safer than the other forms of mechanical irritation employed for this purpose (bougies, bags, or packing). Although the risk to the mother and child is very small, the procedure should be recommended only when there is a definite indication for termination of the pregnancy.

DISCUSSION

DR. LEIGHTON C. CONN, EDMONTON, ALBERTA, CANADA (By Invitation).—The frequency with which this method is used in my country is shown by the following percentages. Of 1,707 general admissions to the Vancouver General Hospital this method was used 51 times. In our own University Hospital, this maneuver was used 94 times in 1,000 consecutive admissions, while in the Royal Alexandra Hospital in a similar series it was performed 17 times. In the Royal Victoria Hospital,

Montreal, through 1,000 consecutive admissions, rupture of the membranes was performed in 75 instances. The latent period in these several series averages 3.5 hours while the duration of labor averages 7.5 hours.

The slides of our own series of cases show the indications for rupture of the membranes to be: preeclamptic toxemia 48 cases, disproportion 38 cases, hydramnios 3 cases, hemorrhage 3 cases, and twins 2 cases. In 16 cases we used rupture of the membranes alone, while in 30 cases we gave a medical induction prior to rupturing the membranes. In 44 cases where medical induction failed, we allowed an interval to elapse before rupturing the membranes; which I think is a mistake. In 4 cases where medical induction followed by bag insertion had failed, the membranes were ruptured to induce labor.

The latent period varied with the procedure used, whether rupture was performed alone or followed medical induction. The duration of labor in our series is greater, I think, than in the cases presented by Dr. Plass. In 20, outlet forceps were applied, while in 13 cases manual rotation of the head followed by forceps application was necessary to effect delivery.

Rupture of the membranes would appear to offer an effective means for the induction of labor but, to me, there are some dangers. In spite of the large number of cases where Dr. Plass used this method in the presence of a floating head, I still believe there will result an occasional prolapsed cord. In the primipara with a long cervix, where one would have to dilate the cervix in order to rupture the membranes, there is a greater tendency for a longer latent period. As Dr. Plass has shown, if there is a longer latent period there is greater danger of morbidity to both mother and child. In these cases we do not perform this method of induction.

In reviewing the records, I was struck with the instances in which, following rupture of the membranes, the interne had noted "tumultuous pain." Is it not safer for the baby in these severe types of labor to keep the head surrounded by the bag of waters so that the pressure will be more evenly distributed thereon?

Moreover, while in the acutely toxic cases labor ensued quickly, in the chronic types of toxemia we had extreme difficulty in getting the uterus to contract. In the latter I prefer the following method: first to insert a bag to secure sufficient dilatation and then, if necessary, to rupture the membranes.

I feel that one should have a definite indication for bringing on labor. In Dr. Plass' hands and in his clinic there would perhaps be no difficulty but, if we were to have this tried throughout the country, I believe that both fetal mortality and maternal morbidity might be increased. We did not lose any mothers in our series and our maternal morbidity, by the same standard, was only 11 per cent. This, I feel, was rather a matter of luck as the number of cases was very small. I would consider rupture of the membranes, where indicated, an excellent procedure, but we must bear in mind that there are times when it is neither safe nor effective.

DR. NICHOLSON J. EASTMAN, BALTIMORE, MD. (By Invitation).—The report of Dr. Plass on the induction of labor by artificial rupture of the membranes has seemed to me most interesting and instructive, for he has disregarded completely what I have always taken to be the two main contraindications to the method, namely, a floating head and a long, hard cervix. In about one-half of his cases the head was floating and in the vast majority the cervix was thick and uneffaced.

When we violate a well-recognized and reasonable contraindication, we expect in a long series of cases to pay a price, and I feel that Dr. Plass has paid a price in his series in the form of five cases of prolapse of the umbilical cord and one case of prolapsed arm. In a series of 303 Baltimore cases quite comparable in other respects to those of Dr. Plass, but in which we were careful not to employ this procedure unless the head was engaged, there was only one case of prolapsed cord. This represents an incidence of 0.3 per cent, whereas in Dr. Plass' series it was approximately 1 per cent. Accordingly, it would seem reasonable to believe that when

we rupture membranes for the purpose of inducing labor in cases in which the head is floating, we impose upon the infant the likelihood of prolapse of the umbilical cord. Now, if the condition prompting the induction, let us say a fulminating toxemia, imposes upon the child a greater danger, this is all very well, and I feel we are very much indebted to Plass for demonstrating the relative safety and feasibility of this procedure under such circumstances. But in the absence of such indications, to rupture the membranes simply for the convenience of the patient or of other persons involved in the case seems to me unjustifiable and at variance with the best interests of mother and child.

Although it is difficult to prove statistically, there is some evidence that the quinine usually employed as preliminary medication to rupturing the membranes may be harmful to the infant, and we have reduced the dosage by degrees from 30 to 20 to 10 to 6 gr. Furthermore, we now have a small series of 50 to 60 cases of labor induced by rupture of the membranes in which no quinine at all was employed; and the procedure seems to work just as well without it. In a series of experimental studies, Schübel has shown that large doses of quinine paralyze the uterus, while small doses of quinine stimulate it; and he finds that the maximum stimulating dose in animals is 1 to 2 mg., intramuscularly, per kilogram of body weight. This would correspond in the human being to a dosage of some 3 to 4 gr. by mouth. In view of this evidence it would seem quite possible to reduce the dose of quinine without decreasing the efficacy of artificial rupture of the membranes, and possibly with some gain in safety to the infant.

DR. CARL BACHMAN, PHILADELPHIA, PA. (By Invitation).—Many obstetricians must feel that Dr. Plass' report, based as it is upon a careful study of so many cases, sets a capping stone upon the evidence which has been accumulating during the past decade in favor of puncture of the membranes. The evidence on the whole would indicate that when this method is applied experimentally by competent men to cases of normal pregnancy at term, it is simple and effective, is probably the safest of the known effective methods of induction, and, barring the accident of prolapse of the cord, entails no serious increase of risk to mother or infant over that to be expected in a comparable group of natural labors.

The studies of Reynolds, Robson and others show that in lower animals uterine motility in pregnancy is inhibited to a marked degree by endocrine factors until shortly before term. Obstetricians have repeatedly experienced difficulty in inducing premature labor. Berger, for instance, with the very method under discussion, found that the latent periods and subsequent labors were usually prolonged when the induction was attempted prior to term. Schulze, furthermore, noted that following spontaneous rupture of the membrane in preterm pregnancies the labors were tedious in spite of the absence of any factors of disproportion or malpresentation.

All of this therefore raises the question whether one may not speak of a necessary irritability or preparedness of the uterus for labor, a condition not arrived at until term. Could the data which Dr. Plass has so carefully analyzed in other respects be recast to correlate the length of the latent period and subsequent labors with the maturities of the pregnancies as indicated by the weight and length of the infants delivered? Would the figures show that prolonged latent periods and labors were associated with the birth of small and presumably preterm infants?

A second aspect of the problem is the view of the lower uterine segment as a trigger zone, stimulation of which serves to induce labor notwithstanding any unpreparedness in the contractile upper portion of the organ. The effectiveness of bag induction in many pregnancies which have to be terminated prematurely is an illustration in point. Also pertinent is the difficulty which many, like Fitz-Gibbon, have reported in inducing even term labor by ordinary medical means when the presenting part, as in multigravidas, is still floating.

Is the effectiveness of simple rupture of the membranes the result of the presenting part descending after the drainage of the amniotic fluid or, since some observers have noted that much fluid drainage is not essential for success, at least by the lower uterine segment having been brought into closer contact with the presenting part?

Dr. Plass' data are exceptionally complete and detailed regarding the level of the fetal head at the moment of puncture of the membranes. It would be of great interest if the records could also tell what happens to the head of the fetus or to the lower uterine segment following puncture, particularly toward the end of the latent period and at the onset of effective uterine contractions.

DR. HARVEY B. MATTHEWS, BROOKLYN, N. Y.—There are several points I would like to make. First, in our clinic, we do not rupture the membranes except on indication. Second, regarding the question of morbidity, Dr. Plass spoke of using 2 per cent mercurochrome. We believe that 4 per cent mercurochrome would cut down his morbidity of 24.5 per cent or that of 9.3 per cent, at least in half. We do not ask him to use mercurochrome, but we do advise the use of some potent germicidal agent, because we are convinced that it has something to do with reducing morbidity and mortality. Last, Dr. Plass did not give us the follow-up on the condition of the cervix in these cases in which the membranes have been prematurely ruptured. Such a follow-up would be very interesting.

Would Dr. Plass express his views on the routine premature rupture of the membranes in private practice? Does he recommend such a procedure to the profession?

DR. ALFRED C. BECK, BROOKLYN, N. Y.—It would be interesting if Dr. Plass would inspect the cervixes of those cases that can be brought back for observation and compare his findings with those made upon a similar number of primiparas and multiparas who have had labors in which the membranes remained intact for most of the first stage.

DR. EDWARD A. SCHUMANN, PHILADELPHIA, PA.—I cannot refrain from taking one moment in this discussion to assist Dr. Plass in answering Dr. Beck's question. In a series of cases we have rather carefully inspected the cervix during and after labor, and we found that our incidence of laceration is slightly less than in the primipara where the membranes have not been previously ruptured. We do not use mercurochrome in the vagina.

DR. PLASS (closing).—This work was done on a completely experimental basis, as a clinical study. Rupture of the membranes is an efficient means of inducing labor, but I believe it should generally be used only in cases where there is an indication for the interruption.

The effect of small doses of quinine, which Dr. Eastman has mentioned, is very interesting. We have always used from 18 to 20 gr., but I am perfectly willing to reduce the dosage to 2, 4, or 6 gr. with the hope that the results may be as good.

I cannot answer Dr. Bachman's question about the latent period in relation to the weight of the baby.

The question of morbidity that Dr. Matthews raised is a perennial obstetric discussion. If he takes temperature as we do his cases are comparable, but if not comparison is unwise. Our temperatures are taken every four hours, day and night. A four-hour nursing schedule is in effect and temperatures are taken at the same time.

A STUDY OF ONE THOUSAND PLACENTAS*

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ALTHOUGH great interest has been shown in the study of placental pathology during the past few years, much still remains to be worked out, and there are still many conditions of the placenta about which there are differences of opinion. A careful analysis of the work already reported by various investigators would probably serve to reconcile some of these diverging opinions, and additional studies of the placenta will surely solve some of the remaining problems. In the hope that additional light might be shed upon this interesting phase of pathology, a combined clinical and pathologic study of the placenta was started in 1934 and has been carried on ever since.

The method of study was as follows: All placentas were examined as soon after delivery as possible and in all cases within twenty-four hours time. After removal of all retroplacental clots and free blood, each placenta was weighed and measured in its smallest and its largest diameters. It was then carefully inspected for any gross abnormalities. The placenta was then spread out on a dissecting board with the maternal surface uppermost and cut through its entire thickness down to the amnion in strips 1 cm. wide. These cut surfaces were examined grossly for abnormalities and the placenta was measured through its thickest portion. It was then cut at right angles to the first series of cuts, so that it was finally divided into blocks 1 cm. square all held together in proper relationship by the amnion and chorion. Sections for histologic examination were taken from appropriate places and prepared by the usual formalin-paraffin technique. It was not possible to prepare histologic sections of all placentas examined. However, care was taken to get a sufficient number of sections from all the different abnormalities noted, and these are still being studied as opportunity permits. The clinical data required to complete the study were then obtained from the hospital records.

All of the patients were white women. The cases were about equally divided between private and ward patients, but, with few exceptions, all were given about the same prenatal care. Practically all of the cases were planned admissions, and all were beyond the twenty-sixth week of gestation. An exceptionally low incidence of clinical abnormalities made this series of cases unusually valuable for a study of the physiologic changes in the placenta in late pregnancy.

*Read by invitation at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

TABLE I. GROSS ABNORMALITIES OF THE PLACENTA

CASES	NO. OF CASES
Infarcts (5 mm. or larger)	416
Placentalos	226
Cysts	116
Hemorrhage	78
Fibrosis and calcification	104
Placentas showing average pathology	650 (65%)
Placentas showing excessive pathology	350 (35%)

A great deal has been written about placental infarcts, and there is still wide divergence of opinion as to their etiology and their varieties. Williams describes six separate types. Siddall and Hartmann describe four distinct varieties, which they simply number for want of descriptive names. My own opinion is that we should divide them into two classes, maternal and fetal, according to the tissue in which the pathologic changes originated and which is, therefore, most involved. The color of the infarct is of no value in determining its origin. Consequently, it is useless to divide them into so-called red and white infarcts. The color of the infarct depends upon a number of factors, chief among which are the presence or absence of hemorrhage into the affected tissue and the time of occurrence of the pathologic change, before delivery. We may, therefore, have an old white infarct of definite maternal origin which is grossly indistinguishable from the more commonly occurring fetal white infarct in which the chorionic villi are chiefly affected. The incidence of infarcts in this series (41.6 per cent) was lower than that reported by most other observers.

During the stage of formation of the placenta and for a short time after a definite hemotrophic system of nutrition is provided for the embryo, the enzyme from the trophoblast liquefies and holds in a state of liquefaction the maternal cells with which it comes in contact. At this stage the trophoblast is markedly invasive, but as soon as the secondary villi are formed and vascularized, its invasive properties slow down and apparently its enzymic action ceases. Up to this point there have been marked destruction of the decidua and lesser injury to the trophoblastic tissue. Wherever tissue damage occurs, it is nature's rule to wall-off the damaged or dead tissue from the adjacent normal tissue. This is accomplished by the deposition of fibrin and the invasion of the area by neutrophils, erythrocytes, lymphocytes, and reticulo-endothelial cells. In other words, the phenomenon known as an inflammatory reaction takes place around or in the damaged tissues. In the placenta, however, the enzyme action of the trophoblast resists this for a time. Likewise the syncytial cells possess the characteristic of endothelium in not instituting clotting of blood. As the placenta grows older, the enzyme action is lost and degenerative changes occur in the syncytial cells, so that they no longer inhibit but now actually cause the deposition of fibrin. This is, of course, the explanation of the formation of Nitabuek's fibrin

layer, but I believe it is also the explanation of the formation of most of the so-called white infarets of the placenta, especially those of rather irregular outline, involving chiefly the chorionic villi. Here the fibrin is deposited in little masses on and under the syncytium of the villi. As a result, the function of the villus is interfered with and eventually it undergoes necrosis. This process, going on simultaneously or progressively in a group of adjacent villi, results in the formation of an infaret which, because of the relative absence of hemorrhage into the affected area, is white from the start. Practically every placenta at term shows numbers of such infarets of various sizes. I believe they represent purely senile changes and, except for the fact that such a placenta, like any other senile organ, is abnormally susceptible to changes from any other disease condition, bear no relation to toxemia in the mother. A striking and, to me, significant feature in connection with such infarets is the relative absence of enmeshed red blood cells in these fibrin masses and the almost complete absence of neutrophiles and lymphocytes around these necrotic areas. If the necrosis occurs sufficiently early in pregnancy for nature to fibrose the affected area, then one sees reticulo-endothelial cells invading the necrotic areas but not in such large numbers as are commonly seen in infarets of other organs, such as the kidney, and not accompanied or preceded by neutrophiles and lymphocytes. I interpret this to mean that such infarets are of a very low degree of toxicity to the surrounding more normal tissue and to the maternal organism.

The deposition of fibrin around senile and consequently degenerated villi is, therefore, the primary factor in the production of so-called white infarets of the placenta, and the endarteritis, thrombosis, and hemorrhage seen in such infarets are secondary to the added interference with villous function by this fibrin deposit.

As the hormonal stimulation of the decidua begins to fail, this structure also undergoes degenerative changes. From a maximum thickness of about 10 mm. at the fourth month of pregnancy, it becomes thinned out to only 1 or 2 mm. at term. Part of this thinning of the decidua is due to the growth of the uterus, but much of it is due to actual regression and degeneration of the decidua. At any rate, it becomes progressively susceptible to traumatism, toxins, and disease conditions in the mother, so that frequently definite damage occurs in this tissue, and because of the highly vascular character of the decidua, such damage usually results in hemorrhage. Provided the hemorrhage is not too extensive, the pregnancy will continue without clinical evidence of the accident, and at the time of delivery, we will find one of the following pictures, dependent upon the time at which the hemorrhage occurred. If the hemorrhage occurred during or shortly before labor, there will be a sharply circumscribed collection of fluid blood of a red or black color somewhere within the placental substance. If the accident occurs a little

earlier, the blood will be clotted and surrounded by a fibrous pseudocapsule out of which the clot may be turned intact like a hard-boiled egg may be removed from its shell. In one case in this series, the clot was so perfect that a tiplike process leading into the maternal blood vessel, from which the hemorrhage occurred, could be clearly seen. When still older, we find the clot partly invaded by fibrous tissue, so that it can no longer be cleanly removed from its capsule. In still older specimens, the clot is entirely penetrated by fibrous tissue, and the color at the periphery is gradually removed until finally, in very old specimens, the entire area is converted into a mass of white fibrous tissue, sometimes with a cavity in the center. The placentas in this series presented all these variations in a striking manner. In no case was the fetus affected so that my findings are in complete agreement with those reported by McNally and Dieckmann in 1923. In many of the placentas showing such infarcts, there were immediately adjacent white infarcts of the type first described. This, of course, might logically be expected. In no case, however, was I able to find an infarct which appeared to be of any other origin.

TABLE II. TOXEMIA AND PLACENTAL PATHOLOGY

TYPE OF TOXEMIA	NO. OF CASES	PLACENTAL PATHOLOGY		FETAL MORTALITY
		AVERAGE	EXCESSIVE	
Nephritic	3	0	3 (100%)	1 (33 $\frac{1}{3}$ %)
Eclamptic	2	1 (50%)	1 (50%)	1 (50%)
Preeclamptic	14	6 (43%)	8 (57%)	5 (36%)
Totals	19	7 (37%)	12 (63%)	7 (35%)

The number of cases of toxemia in this series (19) was too small to be used in drawing definite conclusions as to the relationship between toxemia and placental pathology. I will, therefore, simply state the facts of these cases and the opinion I have formed from them. Fifteen and one-half per cent of our fetal deaths occurred in toxemic patients. There were three cases of nephritic toxemia in this series. In all three there was very extensive pathology in the placenta. In one patient more than two-thirds of the placenta was infarcted. The fetus was born dead. In another, about 60 per cent of the placenta was infarcted, but a living fetus was delivered. In the third case of nephritic toxemia, the placental pathology consisted of marked fibrosis with calcification of the maternal surface of the placenta and a number of discrete scattered placental infarcts, 5 of which measured at least 5 mm. in diameter. In this case also a living baby was born.

One case of eclampsia showed more than the average amount of placental pathology, and the fetus was born dead. The mother also died of toxemia and postpartum hemorrhage. In the other case of eclampsia, the placenta was about as normal as the average, and the fetus was born alive.

Among the fourteen cases of preeclamptic toxemia, there were 5 still-born children, including one set of twins. In the case of the twins, there was marked placental pathology with infarcts and senile changes and very thick, short umbilical cords with small vessels, much jelly of Wharton and almost no twists whatsoever. In the other three cases of preeclampsia in which stillbirths occurred, the placental pathology was of more than average extent, but no greater than that seen in a number of placentas from clinically normal cases with the births of living fetuses. In the remaining 10 cases of preeclampsia, 4 placentas showed more than average pathology, and 6 were of average or even a little less than average pathology. Thus, it is seen that in these 19 cases of late gestational toxemia, there were 7 fetal deaths, 4 of which were definitely traceable to placental pathology. Twelve of the 19 placentas (one fused twin placenta) showed pathologic changes exactly similar to but more extensive than those seen in the average normal cases in this series. The remaining 7 placentas were as nearly normal as are usually found at term. Therefore, the incidence of placental pathology among these toxemic patients was 63 per cent as compared with 35 per cent for the entire series. Although considerable time was spent in studying the histologic sections of these placentas, we were unable to find anything whatsoever that would enable us to state that the section came from a placenta of late gestational toxemia. Even the extent of the gross and microscopic changes was of no value in this respect, because with the exception of the one placenta from a case of severe nephritis, there were just as extensive changes noted in other placentas from clinically normal patients. Two competent pathologists who very kindly examined these sections were also unable to identify which ones came from patients with toxemia and which came from normal patients. It would seem, therefore, that toxemia is simply an additional factor in producing the degenerative changes that occur in all placentas in the last trimester of pregnancy, but that the result may be such extensive placental damage as to cause the death of the fetus.

SYPHILIS

There were no fetal deaths from syphilis in our entire series. In fact, there were only 5 positive Wassermann reactions obtained in the entire 1,000 patients, an incidence of 0.5 per cent. In two of these patients, positive Wassermann reactions were obtained both prenatally and from the cord at delivery. Both fetuses were clinically syphilitic. The other 3 patients gave positive cord Wassermann reactions, but the fetuses showed no clinical evidence of syphilis. In none of these patients were we able to diagnose syphilis from the histologic or gross study of the placenta. The incidence of syphilis in these patients was very low but is accounted for by the fact that we were dealing with married white women exclusively, and all were of a fairly high social and moral status.

All patients had cord Wassermann and Kahn tests done, and all ward patients and most of the private and semiprivate patients had prenatal Wassermann tests in addition.

PLACENTOSIS

The condition of the placenta described by Goodall under the name of placentosis was encountered in 226 patients in this series. In no case could we find clinical evidence of the presence of this condition before delivery of the placenta. Such a placenta presents a gross picture that attracts immediate attention. It is very dark, almost black in color, thicker than the average with swollen, turgid, well-marked cotyledons. The placenta feels soft, friable as though filled with fluid. The fetal vessels are filled with blood. When cut in the fresh state, the contained blood oozes from the cut surface and after draining away leaves a honeycomb appearance in the placenta. Definite areas of hemorrhage are frequently seen in such placentas. To this picture Goodall has aptly applied the term "red hepatization of the placenta." Although such a condition as just described was encountered in nearly 25 per cent of these cases, there was not a single case in which the condition was as extensive or the placenta as thick as those described by Goodall. The thickest placenta in this series measured exactly 4 cm., whereas Goodall reports placentas of 5 to 7.5 cm. in thickness. Furthermore, we did not encounter a single placenta of the large, white, fatty degenerated type which he describes as the end-result of massive and intense placentosis with death of the fetus. It must be emphasized that the cases in this series presented very few clinical abnormalities and that, therefore, the placentas might logically be expected to be fairly normal. Dr. Goodall's series apparently presented a much higher incidence of clinical and consequently of placental abnormalities. Because of these facts, I have been led to interpret this condition of placentosis very differently than he did. My study of these placentas has resulted in a rather definite opinion that the condition described as placentosis is really simple passive congestion of the placenta. I believe it may be produced by toxic conditions in the mother, although I was unable to find evidence of it in this series. I believe the majority of these cases are caused by interference with the maternal blood supply to the placenta and are due to a reduction in the area of the placental site. This may be brought about in several ways, but the condition is probably most commonly due to our method of handling the third stage of labor. In our hospital the routine method of treating the third stage of labor is to clamp the cord with two hemostats and cut between them. Then an ampule of pituitrin is administered by hypodermic injection and the uterus held with firm, constant pressure until evidence of placental separation appears, at which time it is expressed by suprapudal pressure. Now just what is occurring in the uterus and placenta at this time? First, the fetal circulation

is stopped immediately by the clamping of the cord. The function of the chorionic villi may, however, continue for an appreciable time after the cord is cut. Hence the fetal vessels may become progressively engorged, not with additional cells but with serum from the maternal blood sinuses. Second, the maternal portion of the placenta, although most commonly quickly detached from the uterine wall following delivery of the child, may remain attached and therefore continue to function for some time after the cord is cut. Last, the placental site is being rapidly diminished by the contraction and retraction of the uterus. This results in constriction of the maternal vessels in the placental site, but the effect of the constriction is necessarily more pronounced in the veins than in the arteries. Hence blood is still rather freely entering the placenta, but its egress from the placenta is practically stopped. Here, then, we have all the elements necessary for the production of passive congestion of the placenta. Much the same set of conditions prevails in cesarean sections in which it is common practice to administer oxytocics just before opening the uterus and in which there is frequently a sufficiently long interval between the actual delivery of the child and the removal of the placenta for a passive congestion to occur in this organ. Undoubtedly, there are other methods of production of passive congestion of the placenta. Thus premature rupture of the membranes with loss of much of the liquor amnii and consequent diminution of the area of the placental site might produce it. Hence the condition should be encountered frequently in clinics where the Slemmons method of induction of labor is commonly practiced. Likewise, it might be expected to occur rather frequently in that portion of the placenta supplying the second-born child of a twin pregnancy, and this was actually noted in this series of cases. Now if this hypothesis of the production of placentosis is correct, then such a placenta, theoretically, should show the microscopic evidence of passive congestion and such was actually the case. In all such placentas, there is marked engorgement of the fetal vessels and also of the maternal blood sinuses, and the microscopic picture of simple passive congestion was not more frequently complicated by associated, but etiologically unrelated, pathologic changes than would be expected on the basis of the frequency of these associated changes occurring alone. Furthermore, if this hypothesis is correct it should, within certain limits, be possible to control the production of this condition. In an attempt to prove the correctness of this hypothesis, I have been examining a series of placentas from cases in which the treatment of the third stage of labor has been greatly modified. In these cases (all ward cases), a single hemostat is placed near the fetal end of the cord and the cord then is severed and allowed to drain. The uterus is not touched, but the drapes are pulled back so that it may be observed through the abdominal wall. No oxytocics are administered. When there is definite evidence of separation, the placenta is expressed by suprafundal pressure, if necessary;

otherwise it is allowed to be expelled spontaneously. So far, in a series of 43 cases, I have not encountered a single case of placentosis. It is true that only clinically normal patients with normal labors have been utilized for this study, but so far the results bear out my idea that placentosis is simply passive congestion of the placenta which ordinarily is of no clinical importance. However, I fully agree with Dr. Goodall that in the event this condition of passive congestion is present over a sufficiently long period of time before delivery of the child, it may lead to marked definitely pathologic changes in the placenta, such as large areas of infarction, large hemorrhages or even fatty degeneration of the placenta and may so seriously interfere with its function as to cause the death of the child.

SUMMARY

The placentas from 1,000 consecutive deliveries of married, white women beyond the twenty-sixth week of pregnancy were examined grossly in the fresh state within twenty-four hours after delivery. Histologic sections of the abnormalities found were prepared and studied microscopically.

Placental infarcts are classified as fetal and maternal, depending upon the tissue in which the process starts and which is, therefore, most involved. The formation of the placental infarcts is discussed.

A study was made of the relationship between late gestational toxemia, fetal deaths, and placental pathology as evidenced in this series of cases.

The condition known as placentosis is discussed as to its pathology and etiology.

CONCLUSIONS

The occurrence of a high percentage of pathologic changes in the placentas from a group of patients with an unusually low incidence of clinical abnormalities leads to the conclusion that such changes must be considered as senile degenerative changes taking place in an organ whose life span is barely sufficient for the proper performance of its physiologic functions.

The placental changes found in cases of late gestational toxemia are identical with, but occur more frequently, and are more extensive than those found in clinically normal cases. The maternal toxemia must, therefore, be regarded simply as an additional source of injury to an organ already undergoing the pathologic changes incident to senility.

Placental infarcts of the fetal type are due to degeneration of the syncytial cells of the chorionic villi with the deposition of fibrin masses around the villi. These fibrin masses interfere with the function of the villi and so induce endarteritis, thrombosis, and necrosis of the affected villi. An unusual type of low-grade inflammatory reaction occurs around and within the affected tissue and forms the so-called white infarct of the placenta. Placental infarcts of the maternal variety are

due to degenerative changes in the decidua in which, because of its highly vascular nature, hemorrhage is the most characteristic pathologic change. The walling-off and eventual fibrosis of the area form the so-called red infarct of the placenta.

The condition known as placentosis was found in nearly 25 per cent of the placentas in this series. In no case could symptoms or clinical evidence of the presence of this condition be found. It was apparently without effect upon either the mother or the child. The conclusion is reached, therefore, that this condition is one of simple passive congestion of the placenta which in most cases occurs late in labor or even after the birth of the child.

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1900 RITTENHOUSE SQUARE

DISCUSSION ON PAPERS BY DRS. IRVING* AND HARER

DR. A. T. HERTIG, BOSTON, MASS.—In some manner, not always apparent, nature has performed an experiment on these uteri which has resulted in the absence, either complete or partial, of decidua, thereby leading to the clinicopathologic entity of placenta accreta. The study of these abnormal placental sites enables us to evaluate some of the disputed histologic features in the normal placental site since one of the normal elements, decidua, is absent. These disputed points are: the fibrinoid layer of Nitabuch, the placental septa, and the placental site giant cells.

The fibrinoid layer of Nitabuch, as has been shown, is associated with the junction of placental trophoblast and maternal decidua. Furthermore, it seems to be a

*To be published in Surgery, Gynecology and Obstetrics.

product of the decidual cells *per se* because strands of this fibrinoid material from the main layer run down, around, and between the true decidual cells. When the latter are absent, the fibrinoid layer is also absent.

As for the placental septa, there are various ideas concerning their origin. Some authors maintain that they are entirely fetal in origin, others say that they are purely decidual in origin, while still others postulate a combined fetal and maternal origin. It would seem, therefore, that when decidua is definitely absent we have a chance to determine the nature of placental septa. In a large proportion of this series where placental septa were available for observation, these structures were composed of varying proportions of trophoblastic cells from the placenta and smooth muscle fibers from the myometrium. Hence, it would seem logical to suppose that these placental septa are derived, in part at least, from the tissue in which the ovum happens to be embedded. In the normal implantation site it is decidua, whereas in such cases as these of placenta accreta where decidua is partially or completely absent, it is myometrium. This finding would, therefore, favor the view that placental septa are of combined maternal and fetal origin.

The two views about the nature of the placental site giant cells are that they are either of trophoblastic or decidual origin inasmuch as those are the only two types of tissue in that region. Since there are none of the decidual cells found in any given area showing the pure picture of placenta accreta, but many placental site giant cells in the underlying myometrium, it would appear to be very good histologic proof that they are of trophoblastic origin.

DR. ARTHUR H. CURTIS, CHICAGO, ILL.—I would like to ask Dr. Irving whether uterine fibroids are a factor in placenta accreta?

DR. IRVING (closing).—I wish to remark about the point brought out by Dr. Dickinson in regard to the location of the placenta. Beginning with the first of the year we have had the distance from the edge of the placenta to the hole in the membranes measured, in an effort to find out where the placenta is implanted normally. With about 2,700 deliveries a year, eliminating the badly torn membranes, we hope in four or five years to have some information that will be useful.

A review of the literature may throw some light upon the implantation and why placenta accreta occurs. The site was noted in 58 cases. The placenta was implanted in the corpus, which we believe is the normal site, in 19 cases, and at the fundus in 12 cases. It was implanted in the cornua 5 times. There were 10 cases of placenta previa in this group. The whole interior of the uterus was covered 6 times, as it was once in our series. There were 5 cases of diverticulum, one in a primipara, which points to this being of congenital origin. In a museum specimen, it was found implanted in the cornu and septum of a bicornuate uterus.

DR. HARER (closing).—The only thing I would add is that in these cases, the point of rupture of the membranes was noted in each case. This information is available from these 1,000 cases but was not included in the paper.

Passalacqua, N.: *The Influence of Ovarian, Mammary, Placental, Pituitary and Suprarenal Extracts Upon the Hematopoietic Organs and the Blood*, *Monitore ostet-ginec* (Bologna) 8: 18, 1936.

The author considers and briefly reviews the principles of the uteroovarian cycle according to Sfameni, which regulate almost all the functional manifestations of every single organ or organ group in woman during her sexual period of life, during menstruation as well as during pregnancy. From his studies he concludes that the hormonal secretions of single glands or groups of glands of internal secretion, under certain circumstances, also can influence the hematopoietic organs and blood constitution.

A BACTERIOLOGIC STUDY OF 500 CONSECUTIVE ABORTIONS, WITH TREATMENT AND RESULTS*

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THE purpose of this study is to emphasize the importance of the group of organisms, known as anaerobes, in 500 consecutive cases of abortion. Treatment and results will also be discussed.

Krönig¹ recognized and described anaerobic streptococci in 1895. In 1905, Little² reported a case of puerperal infection due to anaerobic streptococci occurring in the service of Dr. Whitridge Williams. The importance of this group of organisms was not recognized until Schottmüller³ reported, in 1910, a series of twenty-five cases with a 50 per cent mortality. He stated that the anaerobic streptococcus is a virulent pathogenic organism and cannot be regarded as a parasite, because once having invaded the tissues, thrombi or blood stream, it has pathologic properties. Schwarz and Dieckmann⁴ reported forty-two uterine cultures in 1925 and corroborated the findings of Schottmüller. In an attempt to show the probable source of the anaerobic organisms, Soule and Brown⁵ (1932) studied the vaginal flora of normal clinic patients during pregnancy and found anaerobic growth in 60 per cent of the cases. These studies were continued and in 1934, Schwarz and Brown⁶ reported an incidence of 83.3 per cent anaerobic organisms in 228 cases of puerperal infection treated in the previous ten years on the Obstetrical Service of the Washington University School of Medicine.

It seemed desirable to study another group of cases and compare results. Such a study has been accomplished on the Gynecological Service of the St. Louis City Hospital, No. 1 (for white patients), in a period of eighteen months (500 cases). The treatment of the patients has been carried out under the direction of the Resident Gynecologist, and the bacteriology has been determined by the Bacteriology Laboratory of the hospital.

Cases with positive uterine cultures were divided into three groups: (1) Aerobic, showing only aerobic growth. (2) Mixed,[†] showing both aerobic and anaerobic growth. (3) Anaerobic, showing only anaerobic growth. Table I shows the incidence of positive cultures and then stresses the predominance of the anaerobic group of organisms.

Table II gives some idea as to the types of abortion encountered. If the doubtful group is considered as probably induced (although not admitted as such), we find that over half of the abortions in this series are likely induced.

*Read, by invitation, at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

†Included in the "mixed" cultures are the cases in which the facultative anaerobes were demonstrated. This was done intentionally, in order to simplify the bacteriological study so that it could easily be applied in a clinical way.

Table III combines the findings in Tables I and II and indicates the relatively high percentage of negative cultures in spontaneous abortions. The very high percentage of anaerobic growth in the cases with positive cultures in all types of abortions is illustrated.

Table IV shows the very low incidence of positive blood cultures and analyzes them according to the types of uterine cultures. It will be noted that one case with an anaerobic uterine culture was found to have a blood culture which showed the presence of *B. typhosus* and the patient was immediately transferred to the Isolation Hospital.

TABLE I. UTERINE CULTURES

	CASES	%
Negative	200	40.0
Positive	300	60.0
Total	500	100.0

Analysis of 300 Positive Uterine Cultures

	CASES	%	COMBINED TOTALS	
			CASES	%
Aerobic	24	8.0	160	53.3
Mixed { Aerobic { Anaerobic }	136	45.3		
Anaerobic	140	46.6	276	92.0

TABLE II. TYPE OF ABORTION

Induced	36.6%	}	55.6%
Doubtful	19.0%		
Spontaneous	43.8%	}	44.4%
Stem pessary	0.6%		
Total of all cases	100%		

TABLE III. ANALYSIS OF UTERINE CULTURES

TYPE OF ABORTION	NEGATIVE	AEROBIC	MIXED	ANAEROBIC	TOTAL CASES	TOTAL ANAEROBES
Induced	56 (30.6%)	10 (5.4%)	69 (37.7%)	48 (26.2%)	183	92.1%
Doubtful	29 (30.5%)	6 (6.3%)	29 (30.5%)	31 (32.6%)	95	90.9%
Spontaneous	115 (52.5%)	8 (3.6%)	37 (16.8%)	59 (26.9%)	219	92.3%
Pessaries (stem)	0	0	1 (33.3%)	2 (66.6%)	3	100%
Total	200	24	136	140	500	

TABLE IV. BLOOD CULTURES

Uterine Cultures	
Negative	0
Aerobic	1
Mixed	6
Anaerobic	1 (Typhoid fever)
Total	8

Table V gives the analysis of aerobic organisms obtained in the aerobic and mixed groups of uterine cultures. Considerable emphasis is given to the rôle played by the various types of staphylococci as frequent uterine contaminants.

TABLE V. ANALYSIS OF AEROBIC CULTURES

	AEROBIC GROUP	MIXED GROUP
<i>B. coli</i>	2	30
Staphylococcus (unidentified)	0	29
<i>Staphylococcus albus</i>	5	15
<i>Staphylococcus aureus</i>	5	10
Sporeforming bacillus	7	14
Diphtheroids	0	12
Nonhemolytic streptococcus	1	11
Hemolytic streptococcus	2 (2 died)	7 (2 died)
<i>Streptococcus viridans</i>	0	0
Diplococcus (unidentified)	0	2
Gonococcus	0	2
Yeast	0	1
Not classified	2	3
Total	24	136

TABLE VI. HOSPITALIZATION AFTER TREATMENT

UTERINE CULTURES	CASES	AVERAGE DAYS
Negative	200	5.8
Aerobic	24	5.5
Anaerobic	140	6.6
Mixed	136	7.4
Total	500	6.3

TABLE VII. DIAGNOSIS AND TREATMENT OF PUERPERAL INFECTION

1. Differential diagnosis.
2. Preparation of patient: do not catheterize because of danger of urinary infection.
3. Intrauterine culture and examination of patient.
4. Emptying of the uterine cavity of débris with patient in seminarcoosis, but without anesthesia by: <ul style="list-style-type: none"> a. Foerster's sponge-holding forceps. b. Uterine wiper.
5. Intrauterine douche with KMnO_4 (1-1,000) at 110° to 115° F., under 15 cm. of water pressure or less (irrigating can resting on symphysis), using a large size Bozeman intrauterine douche cannula.
6. Administer ergot preparation, but avoid pituitary preparations.
7. Follow-up treatment: <ul style="list-style-type: none"> Semi-Fowler position. Ice-bag to lower abdomen. Ergot preparations. Rapidly increasing diet (if no peritonitis). Low pressure vaginal douches, KMnO_4 (1-1,000) beginning the third day. Start getting up on fourth or fifth day. Transfuse for anemia.
In cases with signs of peritoneal irritation: <ul style="list-style-type: none"> Nothing by mouth. Intravenous glucose. Subcutaneous saline. Transfusions, large and frequent. Wangenstein apparatus. No laxatives. Daily tap water enema.
8. If temperature remains elevated reexamine every second or third day to determine presence of pelvic thrombophlebitis or beginning pelvic abscess formation.
9. Patient discharged at end of one week under conservative instructions.
10. Reexamine in two or three weeks.

Next in frequency is the *Bacillus coli*. The incidence of the *Streptococcus hemolyticus* is very low, but when it is the offender, the mortality rate is high. In two cases the gonococcus was cultured as the offending organism.

Table VI illustrates the very short period of hospitalization required after treatment. This point is of great interest both to patients and the hospital administration.

TREATMENT

The treatment of puerperal infection has been divided into (1) conservative and (2) active. It appears that the conservative method would be an active method of treatment as has been used in this series of cases. In other words, the inactive treatment is not always conservative, because it may permit the spread of a local infection.

When a patient in the puerperal state develops signs of infection, which cannot be accounted for after the usual diagnostic methods have been used to rule out all other possible infections, then it seems justifiable to investigate the uterine cavity.

The surgical principles involved in the treatment of this series of cases are (1) drainage of an infected wound site and (2) débridement of a potentially infected cavity. This is done with a minimal amount of manipulation in order that further trauma may be avoided. We have demonstrated that this procedure can be safely performed by a junior interne under proper supervision. A general anesthetic is not to be used, because this would remove the inhibiting influence of the patient's response to pain which is usually indicative of too active manipulation. The patient should be under the influence of some sedative so as not to be too apprehensive. Morphia ($\frac{1}{6}$ gr.) with hyoseine hydrobromide (0.0005 gm.) followed by hyoseine (0.0005) in forty-five minutes are given so that the second dose is given at least thirty minutes before the patient is prepared for examination.

The perineum is prepared with 5 per cent neutral acriflavin in 10 per cent acetone and 50 per cent ethyl alcohol. The bladder is *not* catheterized because of the danger of contamination which may frequently superimpose a urinary infection. Drapes are placed. A Graves' vaginal speculum is used to obtain exposure of the cervix. If this is not satisfactory, large vaginal retractors will be necessary. The vagina and cervix are then prepared with the above solution of 5 per cent neutral acriflavin. Treat the cervical canal with this solution, then dry carefully with sterile gauze. A culture is then obtained from the uterine cavity with a modified Little tube. If it is not possible to have careful bacteriologic investigation of the material obtained, at least several smears of the material can be made and stained by the Gram method. This has been done routinely and found to check very well with the bacteriologic findings. Both aerobic and anaerobic blood agar slants should be made. The Wright anaerobic technic is used in search for anaerobic organisms.

After the culture has been obtained, a gentle bimanual examination is done to determine evidence of any spread of the uterine infection, pelvic abscess or thrombophlebitis. This is also done without an anesthetic in order that the patient's reaction to pain will limit the extent of the examination. Too much pressure will not be used, which might cause rupture of an abscess internally. The uterine cavity is very carefully investigated with a Foerster's sponge-holding forceps, plain jaw. Dilatation of the cervix is usually sufficient to permit this. The sponge forceps is inserted closed to the depth desired, opened, closed, and removed to see

if any tissue has fallen within the jaws. The forceps should not be advanced with the jaws open, because of the danger of grasping the uterine muscle. The uterine wall is next explored very systematically and with great gentleness by means of a "uterine wiper" (formerly called a vaginal depressor) much as a windshield wiper wipes the surface of the windshield, without marring the surface. (NO curettage is done.)

The uterus is usually found to be relaxed in such cases. After mechanical removal of any retained débris, the patient is given an intrauterine douche using a Bozeman's extra large intrauterine douche nozzle. This instrument permits the free exit of the solution from the uterine cavity without any pressure being established. Two liters of a 1:1000 solution of potassium permanganate in sterile water at 105° to 110° F. are used. This solution is usually acidulated with 50 c.c. N/1 sulphuric acid. The bottom of the douche can is held at the level of the symphysis so that the water pressure of the solution as it enters the douche nozzle is 15 cm. or less. Such a douche results in (1) removal of small bits of tissue remaining after mechanical emptying of the cavity, (2) firm contraction of the uterus, including the cervix, so that bleeding is controlled and the sinuses are closed, (3) elimination of the putrid discharge which is characteristic of the anaerobic infections.

Table VII outlines the treatment and postoperative care.

We agree with Schottmüller that the manner of spread of such contamination is by way of the endometrium; the organisms invade the uterine wall, parametrium, and thrombosed veins. Therefore, the earlier the local endometritis is treated, the more prompt is the cure. Less complications develop and the period of convalescence is much shortened. The possibility of future sterility is greatly lessened as evidenced by patients returning shortly with another abortion and others presenting themselves for delivery at term. The thrombosed veins in contradistinction to the circulating blood offer a fine culture medium. The proliferating organisms desire hemoglobin as their food and low oxygen tension in their environment. These organisms usually have a definite proteolytic tendency and are able to disintegrate thrombi so that small particles break off and gain access to the blood stream and other organs, particularly the lungs.

TABLE VIII. MORTALITY

TOTAL CASES	TOTAL DEATHS	PERCENTAGE
500	7	1.4
Six of these cases had serious inflammatory complications upon admission and the seventh was almost exsanguinated.		
TYPES OF UTERINE INFECTION		BACTERIOLOGY OF FATAL CASES
Aerobic	2	<i>Staphylococcus aureus</i> 1 14.2%
Mixed	4	Anaerobic streptococcus 2 28.5%
Anaerobic	1	Hemolytic streptococcus 4 57.1%
	7	7

The *Streptococcus hemolyticus* was cultured from the uterus in 9 instances among this series of 500 cases—an incidence of 1.8 per cent. Only 4 of these cases terminated fatally—a mortality of 44.4 per cent.

The proteolytic properties of anaerobic streptococci probably are responsible for the marked loss of hemoglobin in patients with this type of infection. Therefore, one is able to see the rationale of large and frequent blood transfusions in the treatment in such cases. Since treatment has been instituted at an earlier time in the course of the infection, the demand for transfusions has greatly diminished. The

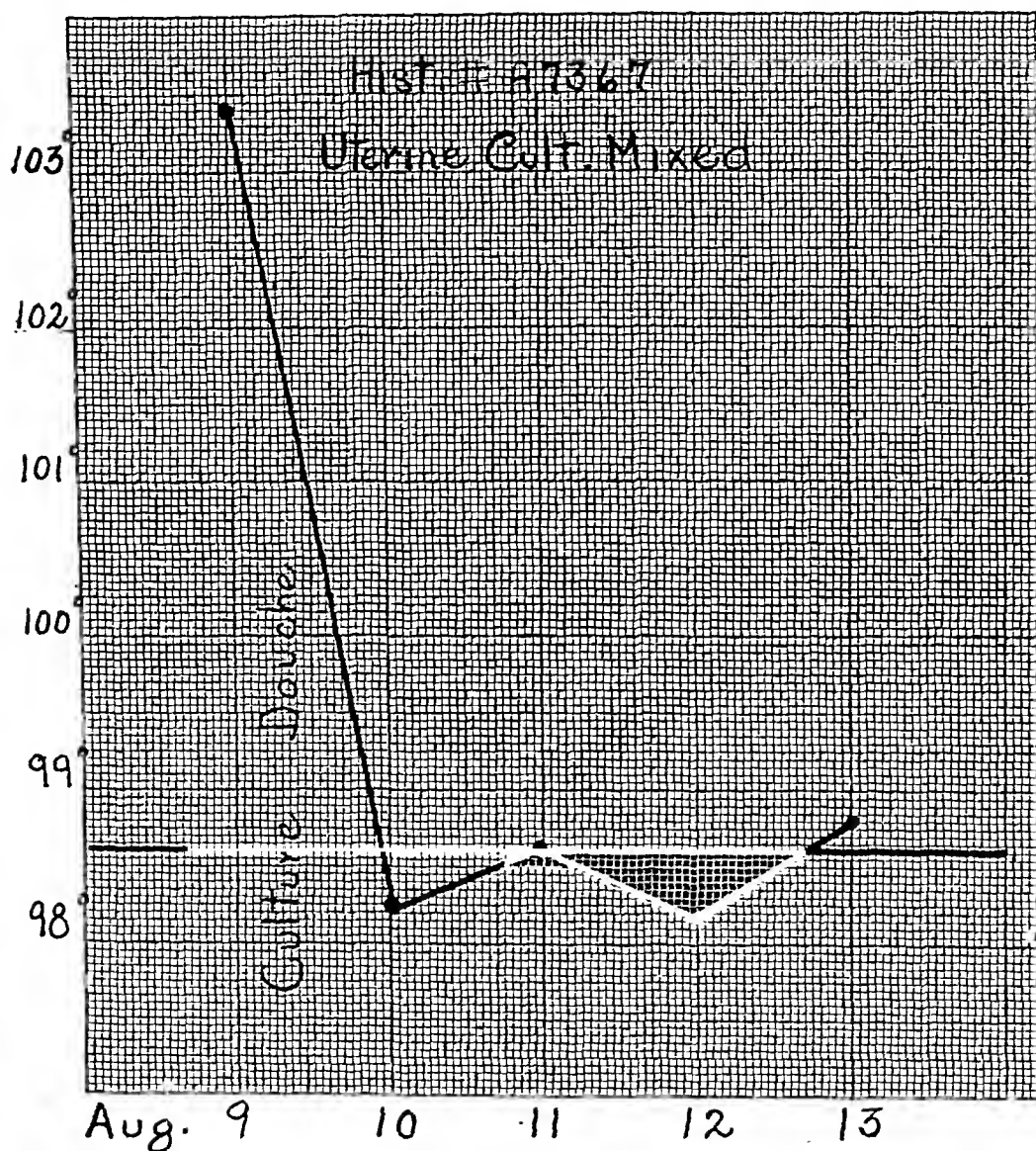


Fig. 1.

disease seldom runs the prolonged or chronic course formerly expected. Leucopenia is a common finding in cases of puerperal infection which are uncomplicated.

RESULTS

Fig. 1 illustrates a typical temperature chart, with the prompt return to normal after treatment.

Table VIII outlines the mortality figures and we observe the hopelessness at the time of admission of the patients who died. The cases are analyzed as to type

TABLE IX. DEATHS

HISTORY	TYPE OF ABORTION	BLOOD CULTURE	COMPLICATION	TRANSFUSIONS	TYPE OF INFECTION	CAUSE OF DEATH (CHECKED BY AUTOPSY)
F. H. 11653 32 days	Criminal (Midwife)	Neg.	Pelvic abscess	8	Anaerobic (Anaerobic Strep.)	Peritonitis Multiple lung abscesses
P. C. 11311 1 day	Self-induced (Catheter 30 da.)	Pos.	Septicemia	0	Mixed (<i>Staph. aureus</i>)	Septicemia
E. S. 17104 24 days	Criminal (Midwife)	Pos.	Peritonitis septicemia	4	Mixed (Hemolytic Strep.)	Septicemia Peritonitis Lung abscess, Lt.
N. J. 19808 12 days	Self-induced (Catheter)	Neg.	Exsanguinated	2	Aerobic (Hemolytic Strep.)	Peritonitis Multiple lung abscesses
D. W. A-4031 3 days	Self-induced (Medicine dropper)	Pos.	Peritonitis septicemia	2	Mixed (Hemolytic Strep.)	Peritonitis Septicemia
S. G. A-10239 13 days	Criminal (Midwife)	Pos.	Peritonitis	4	Mixed (Anaerobic Strep.)	Peritonitis Perforation of uterus
N. S. A-17168 8 days	Self-induced (Catheter)	Pos.	Septicemia	3	Aerobic (Hemolytic Strep.)	Septicemia Early pneumonia

of uterine infection and also as to the predominant organism. The relative unimportance of the *Streptococcus hemolyticus* as to morbidity is stressed, and then its great importance as to mortality is emphasized. The situation in this particular type of infection is by no means hopeless and treatment should be similar in all types of cases, irrespective of bacteriologic findings.

Table IX analyzes the fatal cases, showing the hospital days and other important findings. Autopsy was obtained in every instance to check the cause of death.

CONCLUSIONS

1. Anaerobic organisms play a predominant rôle in the bacterial contamination of the uterine cavity following abortion as they are shown to be present in 92 per cent of the patients with positive cultures in this series of 500 consecutive cases.

2. This finding has been obtained by a different group of clinical assistants aided by another laboratory corps, but checks very closely with the findings of the Department of Obstetrics and Gynecology of Washington University School of Medicine.

3. Sixty per cent of uterine cultures are positive.

4. The incidence of *Streptococcus hemolyticus* as the infecting organism was very low (1.8 per cent), but its importance as a factor in mortality (57.1 per cent) must not be overlooked.

5. The small number of positive blood cultures should indicate its minor importance as a diagnostic sign. It means much more as to prognosis.

6. The period of hospitalization is very short, average 6.3 days after treatment.

7. Treatment should be early and active—culture, gentle evacuation of the uterine cavity, followed by an intrauterine douche.

8. Cases coming to fatal termination were moribund upon admission.

(I wish to express my thanks to the Resident Staff of St. Louis City Hospital, No. 1, for their excellent cooperation.)

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DISCUSSION

DR. WILLIAM J. DIECKMANN, CHICAGO, ILL.—In evaluating the management of abortion cases we have always considered only the mortality. In his closing remarks I hope Dr. Brown will say something about the follow-up of these cases with reference to subsequent sterility, incapacity, subsequent abortions, and ectopic pregnancy as a result of the infection, and something about fibrotic uteri that may develop due to the subinvolution.

The importance of anaerobic streptococci is shown by his report. Whenever uterine cultures are grown both aerobically and anaerobically, it is noted, usually with surprise, that the majority of the organisms are obligate anaerobes. At the Queen Charlotte's Isolation Hospital, where some of the best research work on puerperal infection is being done, about one-third of the infecting organisms are anaerobic streptococci. At the Chicago Lying-In Hospital, our incidence of abortions is small, but it is interesting that in a group of 25 cases of postabortal and puerperal infections, ten or 40 per cent were due to anaerobic streptococci. In 70 uterine cultures, 40 per cent were anaerobic streptococci, 14 per cent mixed and, a very interesting thing, only 6 per cent hemolytic streptococci.

In the subsequent discussion, I hope that the question of radical versus conservative treatment will not be introduced. What Dr. Brown has done is not radical. Adair and Davis in their work on the ergot preparations have introduced bags into the uterus in more than 300 patients with no patient having a temperature of 38° for longer than twenty-four hours. Koff at Johns Hopkins introduced a bag in 70 cases with only one patient developing subsequent puerperal infection. The uterus can be invaded without danger, if proper technic is used.

I think it is of importance to know what type of organism is present, and particularly with the anaerobic streptococci to remove the fragments of placenta that are left. It is not a curettage that Dr. Brown has advised. The purpose of the douche is to stimulate the uterus to contract. There is no hope of washing out the bacteria.

DR. OTTO H. SCHWARZ, St. Louis, Mo.—Various maternal mortality reports have stated that the number of deaths from puerperal infections was entirely too great and that the cause of these deaths was entirely due to neglect. I have maintained that such a sweeping statement was a mistake, because anaerobic infection would occur in many cases whether or not the patient was contaminated.

Puerperal infections are due to two types of organisms, those harbored by the patient and those that are introduced. The anaerobic are the chief cause of the endogenous infections. They can develop under certain conditions and can cause all the conditions of pathogenicity, and our problem today as obstetricians is not so much in preventing the exogenous infections by good technic as in preventing these endogenous infections. Nevertheless our problem is still twofold, the endogenous and the exogenous infections. Of course, with bad technic the exogenous prevail, but with good technic it is the endogenous infections that we must bear in mind. When we do as Dr. Brown has done we shall see fewer cases of puerperal infection in well-regulated maternity hospitals.

DR. BROWN (closing).—That the infection is favored by inadequate drainage is demonstrated very thoroughly in the many cases that we have had. If we can establish drainage, get the blood clots out of the cervical canal and empty the uterus, the patient responds very quickly with a normal temperature and no complications develop.

We have had no serious complications in these 500 patients treated by this method. We have had patients come back after several months with subsequent abortions, and quite a number of patients return within a year for delivery. We do try to educate the patient against the use of abortion, not by preaching but by trying to show the dangers. Many of them come back for subsequent delivery, which I think is of some aid in the lowering of maternal mortality.

Subsequent examination shows the pelvis to be absolutely negative without masses, tenderness, or induration, and the menstrual cycle returns to normal. Since the early

treatment of these patients, thrombophlebitis is almost unheard of. The patient either comes in with it already developed or she does not get it.

Transfusions have been diminished in number tremendously since active treatment. The patient immediately improves, and she regenerates her blood very quickly as soon as the infection and bleeding are arrested.

We do not do a curettage. We empty the uterus and wipe very, very gently. I do not believe in wiping with the fingers because in doing so it is necessary to push the uterus down in order to reach it and get the finger in. In doing this you will squeeze the uterus as a sponge and disseminate the infection.

SIMILARITY IN CERVIX OF RHESUS MONKEY AND WOMAN*

ROBERT L. DICKINSON, M.D., F.A.C.S., NEW YORK, N. Y., AND

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(From National Committee on Maternal Health, Inc., and Carnegie Institution of Washington)

TO JUDGE by thirty adults in the colony of the Carnegie Institution in Baltimore, examined March 6, 1935, the difference in form and pathologic behavior between the vaginal portion of the cervix of the macaque and that of woman is almost altogether one of size, a matter of four-tenths in diameter. Hence, in this field biology and gynecology may find teamwork profitable.

To permit easy visual comparison, drawings to scale were made by one of us (D.). These have been set over against examples in women, each opposite a human cervix which, by employing the above average, is scaled down to that of the monkey. The human types were selected from more than a thousand sketches in the office records of the senior author of this report. These cervix drawings had been made from life, usually life-size, duly checked by measurement, and often in color. This habit developed because of the experience of fifty years that much time could be saved by making life-size sketches as compared with writing entries. By visualized comparison, the similarity is here shown to be astonishingly exact, so much so that, in the accompanying figures, one will not be able to tell which is which save in four instances. *The human and the simian portio vaginalis will be seen to agree in conformation and invagination, laceration and inflammation, eversion and erosion, secretion and vascularity, infantilism and asymmetry.* Cystic degeneration and polyp, cancer and certain infections alone were missing in this short series.

Three differences appear. These are:

1. Facile dilatability of the untorn lower cervical canal and of each external os, a condition almost unknown in women.

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

2. Corrugation of the surface in several instances, with the vaginal rugae covering the anterior lip, or both lips, quite to the external os, a very rare finding in women.

3. Adhesion of the seminal plug to a circular rim of the most projecting part of the portio, not seen in women (Fig. A, 1, 2, 3).

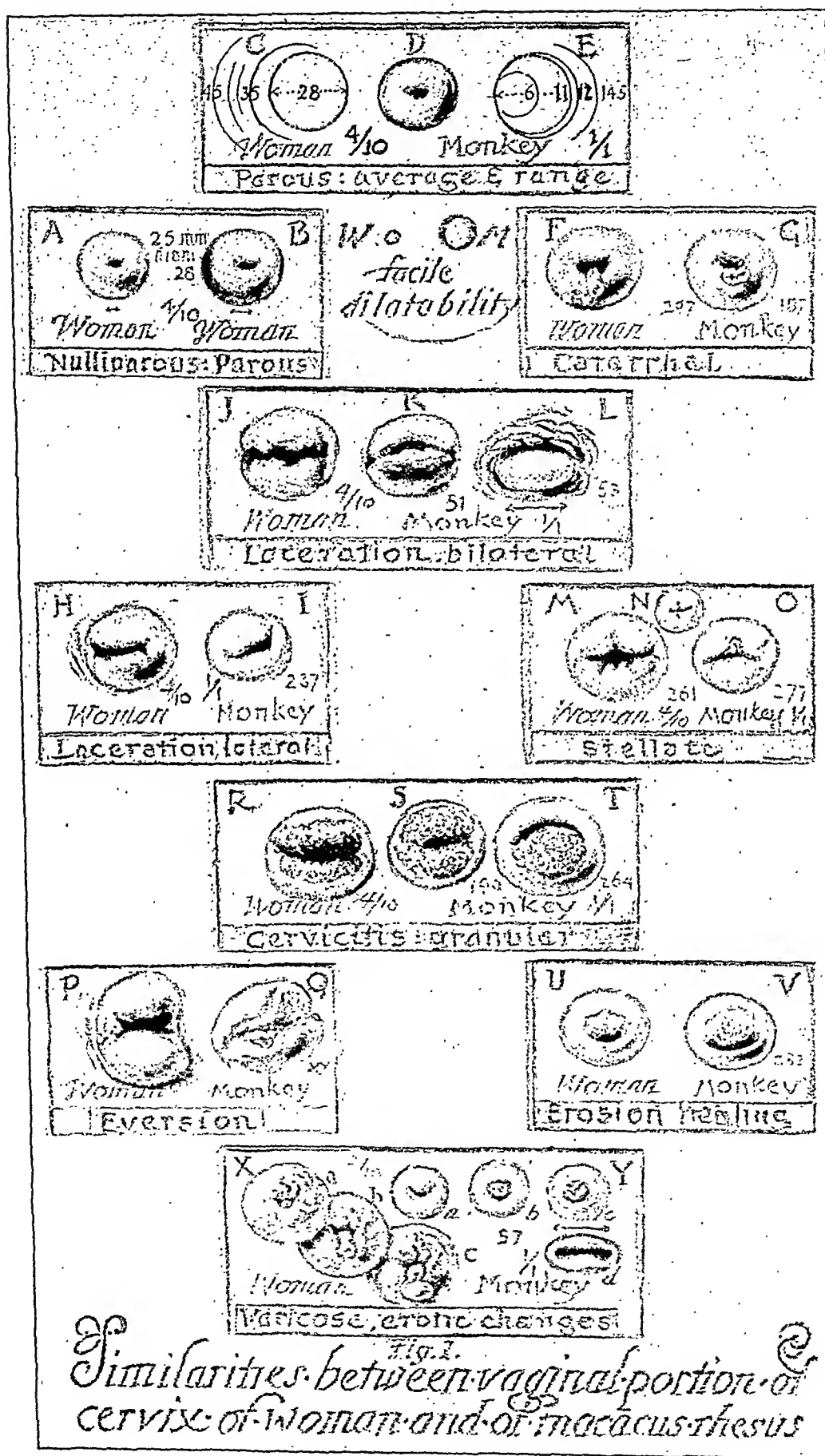
The vagina is worthy of detailed study. It was noted that in 22 instances there was a range from relaxed walls, quite smooth, in a third (C 2, 235), through fine laid rugae in another third (C 2, 73) up to a striking kind of pointed, rigid, almost rasplike points and ridges, in the remainder (C 2, 2). Some walls were very inelastic. As in women, the anterior wall had more corrugated surfaces than the posterior and the lower more than the deeper section. The posterior fornix was deep in an animal one would suspect of vigorous attention from a well-built male, if one drew an inference from the human female.

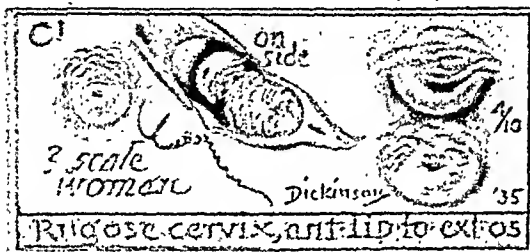
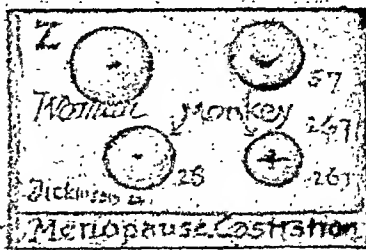
There is a range of color from white (4 cases), even chalky white, through pallid (1) grayish (1) to faint pink (5). This marked lack of color is hardly seen in women. One was purplish, the "erotic" human type, with smooth vagina, prominent clitoris and large wrinkled prepuce.

CLITORIS

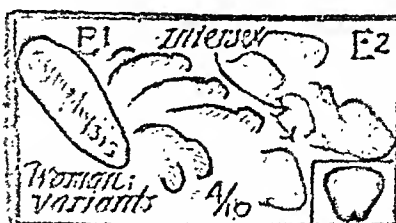
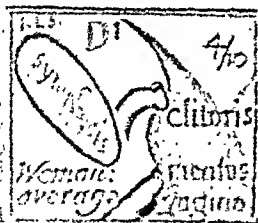
The clitoris of this and other monkeys calls for drawings of larger size, with indication of scale and with detail not given in the literature, even in that of Bolk and Pocock. It is noteworthy that in our few macaques there is exhibited more range of variability in this organ than has been shown in the human beings in the Dickinson Atlas, which exhibits far the largest variety in shape and size in vulvas, yet published, and includes a series of measurements and drawings of the clitoris. As in women, so in the rhesus monkey, there is a wide divergence in dimensions of the clitoris, in location, in axis, in alterations in axis during erection, in erectability, in the location of the prepuce and the amount of preputial corrugation, the latter raising the question of persisting digital frictions in rhesus (E 3, 4). The special traits were a pigmentation not seen in women, blackish, bluish, or purplish; a prepuce far up the shaft, and a relatively much greater projection, resembling a miniature stubby penis or the intersex organ of the human being. In this observation the clitoris was not regularly measured or drawn, but a sample is shown in E 3, where, in the same bracket, a comparison is made with the organ of other monkeys which Dickinson sketched in the Yerkes group at New Haven.

The clitoris of the little spider monkey (Bolk '07, 307) shows the same size (6.5 cm.) and same slit as the intersex clitoris of the woman who lived as a male dock porter, shown in the Dickinson Atlas, Fig. 117. The *Ateles* monkey, however, lacks erectile tissue in its huge clitoris.





Vaginal folds turning to the external os in women & monkey



E3 rhesus
from above
& from side
and pointed
condad; 5,
in body axis



6 baboon
7 gibbon
8 Jap. ope
9 Mangrove
10 Chimpan
11 Zec. 3.5 id.
12 Beneath

Variety of form, size and axis of clitoris in woman (also intersex) & monkeys

CERVIX

For the cervix there were 27 monkeys on which the part could be conveniently measured and depicted. There were 8 of the type typical of the parous woman, namely with a small transverse slit (Figs. B, D, F). Except when torn, anterior and posterior lips were about equal in anteroposterior diameter. Then there were 9 with considerable lacerations, showing all of the human varieties, unilateral, bilateral, stellate and crescentic, the convexity of the latter either caudad or ventrad, and there were tears running out to the vaginal wall (Figs. H to V). Eversion ran true to familiar human types. Cervicitis was again an interesting miniature, ranging from mere mucus catarrh or marked redness, mainly of the slightly everted canal, to granular erosion bleeding at a touch, the lip or lips involved being swollen and outrolled (G, S, T, V, C 2, 303). There was in one sterile animal a conical cervix with pinhole os (and a relatively narrow corpus which did not undergo the monthly cycle of broadening, Wislocki 1932, 217) resembling arrest of development as found in the clinic. Here also was seen our familiar picture of the dwindled portio of age, a year after the animal's castration, or after cessation of ovulation. One cervix was rigid and undilatable as in women (Z 28); one dilatable its full diameter (Fig. Y, d). There was not even missing what Dickinson calls the erotic cervix, with prominent veins and outpouring mucus, changing in vascularity, size and hue, becoming dusky as one watches (Y, a, b, c). The illustrations will show better than words the wide variety in the clinical evidence of childbirth and of rate of involution, possibly of sex excitement.

The average external diameter in this group was a little over 11 mm. The eight healthy cervixes of parous animals plus the six wrinkled cervixes, adding those torn but not thickened, 19 in all, averaged 11 mm. (Fig. E). The comparative range in diameter was somewhat less than among women (Figs. E and C). (Reporting 3 specimens, Wislocki, '32, 171, gives for the whole uterus, 40 mm. length; 18 mm. breadth; 14 mm. thickness, and for the cervix 16 by 12 mm., 16 by 8 mm., and 15 by 10 mm.)

There were five injured or inflamed cervixes running to 14 or 15 mm., and three sterile or atrophic anatomies of 5.5 to 6 mm. (Figs. E, W, Z).

Laceration was evident among the twenty-two monkeys known or thought to have delivered babies, being definite or pronounced in nearly one-half of these. Cervicitis was present in one-fifth of the fully developed organs; with three striking examples of large areas of roughened redness, two being shown in S, T. Rugose or plicated surfaces on the portio occurred in more than one-fifth (C 2), completely covering the area from vaginal wall to external os in three. Invagi-

nation was noted as slight or absent in five cases, and this defect was sometimes accompanied by a wrinkled surface.

Dilatability was noteworthy. Gentle testing showed, among eleven untorn cervixes, on the average, a distensibility equal to half the outside diameter (underneath Fig. D, also Y). This is more than double the relative capacity of the human cervix, even where the powerful leverage of the branched dilator or the push of graduated tapering dilators is brought into play. It is as if the undamaged human canal would, with slight pressure, admit the average male little finger. Of these eleven canals three could be easily opened to 8 mm. and one to 6 mm., or as if the unlacerated, fully involuted cervix of a nonpregnant woman allowed the thumb to pass. Indeed one monkey cervix of 8 mm. external diameter permitted an 8 mm. passage (Fig. Y, *d*) and two of 8 mm. dilatation were in cervixes of 10 and 11 mm. outer diameter. If women were like this, emptying the uterus in early pregnancy by passing a finger would be simple, whereas it is not feasible without damage or incision. Abortion, by separating the ovum from the uterine wall with a (sterile) finger nail as curette, guided by the sensitive finger tip, would be too easy.

The corrugated cervix, or rugose portio vaginalis, shows part or all of the surface looking like vaginal wall, but usually with distinct rounded projection into the vault of the vagina. It suggests an incomplete process of invagination, or smooth-stretching of the epithelial covering, or else arrest of development. In human fetal development and in childhood this ridged surface may be detected (Bayer). The rugae were transverse or crescentic in all but one of the seven, and on both lips in three. In one the folds pointed to the os.

Wislocki says (1932, 174) of the rhesus monkey "the orifice is situated near the ventral border of the cervix so that the dorsal lip is approximately twice as thick as the ventral one. . . . The vagina is lined by coarse longitudinal rugae covered by a multitude of delicate transverse plicae. In the fornix the plicae become longitudinal and extend into the cervix, much more pronounced, however, on the small, ventral lip than on the dorsal lip, which in some specimens is nearly smooth. The plicae converge toward the external os which they enter" (Sic). His gorilla, shown in Broedel's beautiful drawings, presents a cervix which looks a bit like C 2, 2. Wislocki declares (175) that the cervix "is an extremely variable structure in the Simiæ, occurring in the catarrhine and platyrrhine (American monkey), at times in even more differentiated form than in the anthropoids and men." Dickinson draws attention to the fact that in the older museum specimens of the cervix, vagina, or vulva, and even in the large and remarkable Hoffman-Haberda Vienna medicolegal exhibit of external genitals, the surfaces are puckered and therefore distorted. This is particularly true of the Bischoff lithographs with their generally corrugated surfaces as compared with Dickinson's long published series drawn from life, his unpublished drawings and the Heitzmann lithographs of the cervix.

Wislocki (1932, 174) describes the rugae of the cervix of various monkeys as well as the degree of invagination. In the spider monkey, the cervix is large and prominent, with radiating rugae. In the capucine, the howling monkey and the Titi monkey, it is provided with rough excrescences; in the marmoset with an orifice

delicately fimbriated. The gibbon and the night monkey show "no circumvallation, the cervix passing unsignalled into the cervix (meaning vagina?) as a funnel shaped passage, the lips of which are thrown into delicate longitudinal leaflets or fimbriae."

In our 27 monkeys there were seven instances of rugose portio, ranging from small areas to complete coverage (Figs. 1, L, and C, 2). In women only three drawings of such findings are found, so far, by Dickinson, among routine sketch records of the cervix, among his nearly 5,000 retained office histories (Fig. 2, C, 1). No rugose cervix occurs in the only considerable and important published collection of pictures of the cervix, the Heitzmann lithographs in color, 113 in number. Jayle's series has missed this also, among his 33 shrewd observations, unless his Fig. 299, page 501, on a woman of twenty-four, which he calls atrophy, is defective development with its smooth anterior lip, or Fig. 296, page 499, first seen at thirty-five, with no invagination and no projection, as in the monkeys. W. T. Kennedy and J. W. Davies of New York each observed a patient with this conformation after Dickinson had posted a drawing on the bulletin board of the Woman's Hospital.

The cervicitis shows the same range as in women, with like out-rolling and swelling, and the mate of the rather frequent type where, after crescentic injury, one lip is larger than the other and alone eroded (Figs. T, V), it being either anterior or posterior. Even a cyst high up the canal is reported in the gorilla (Wislocki, 1932). In Case XX (Fig. Q) we see subinvolution, where there was voluminous discharge of clear mucus noted. The fertility of rhesus in captivity (35 per cent) might be raised by curing the cervicitis. From rhesus, the gynecologist could well develop clues or tests from the relation of cervicitis to sterility or to general health, to ovulation in particular and to stages of the cycle; with the bacteriology of cervicitis in the monkey; and results from various treatments.

Joachimovitz shows some fine sections of the cervix and corpus.

MEATUS

The meatus might be of importance to gynecology because of the rebellious infections found there in women and the need of experiment in animals. Jayle (1918) and Dickinson (1904, 1933) have pictured its form, but the former ignores, on page 407 and elsewhere, the meatus glands, while at the same time proving the best of sources as to location and number of the vestibular glands.

Wislocki found in rhesus at the meatus urinarius two papillary folds, and in a guenon monkey, slight folds guarding the meatus, none in the anthropoid. He denies them to women (194). I (D.) have pictured and described the frequency in woman, also a monkey or fetal type of urethral opening almost or quite on the vaginal wall (1933). Jayle

shows the rounded projection of the meatus in women, resembling that of some monkeys—a condition of which the student of monkeys seems unaware.

The illustrations in very many of the Simian reports are on such a small scale that the cervix is hard to study. The general absence of indications of scale is notable and surprising. Wislocki is careful in this matter and specific beyond other authors concerning the surfaces of the cervix and vagina (1932, 173, 175) and appreciates the variants that may occur within a given species.

As a clinician, the interest of the gynecologist in these animals leans toward practical considerations rather than toward comparative anatomy. Here the size, cheapness, readiness of domestication and relative fertility of a given animal count heavily in matters of research looking toward improvements in human diagnosis and treatment. The rhesus meets most of our needs, except for the flap (Klappe) closing the canal, and rendering the cavity of the body of the uterus inaccessible, save, apparently, at certain times. I found very marked differences in depth of penetration when trying to test the dilatability of the cervical canal with a forceps, with the tips closed when passed, then spread as wide as the blades would open easily.

CERVICAL CANAL

The cervical canal of the rhesus monkey shows an extraordinary sigmoid sweep, the "two nearly right angled turns" of Wislocki. This "flap" (or Klappe) is shown in A 2. There are two pockets, or more, according to Joachimovitz (1928, 531, 470). He says this deflection is perhaps a stage of the cycle, accompanied as it is by increase of mucus and enlargement of glands, and has clearly pictured the condition. He declares that this transverse fold may stand out in women, particularly in infantile and old uteri. He observed two women with it in adult life and calls it "an infantile stigma." Certainly the gynecologists of the eighties who probed the cavity of the uterus in every case found canals refusing to allow the sound to pass where previously it had slid in easily. I (D.) accounted for this by spasm with tenderness at the internal os in some cases, by large new high cysts in others (Atlas Fig. 34), by inflammatory swelling in others. Yet there were cases inexplicable, which a variable transverse fold would have accounted for. This condition must not be confused with anteflexion, nor with the postmortem slump and crook common in the frozen sections (Atlas Fig. 21). It does, however, handicap our use of rhesus for biopsy of the cavity of the body where it blockades entry.

The comparisons made above, though few and sketchy, suggest new tests, on these eroded surfaces, by implantation of some virulent strain

of gonococcus, because research and treatment of that unconquered scourge, gonorrhea, is gravely handicapped for lack of an experimental animal. The other human habitat of the Neisser germ, the pair of glands at each side of the urinary meatus, might be searched for and injected, if found in the rhesus monkey. A pair of glandular openings are found on each side of the meatus in the gorilla by Wislocki (1932, Plate II, C).

The form of the speculum, not Sims, but simian, for the purpose of examination of the cervix and vagina, may be either tubular or bivalve. A kind of Kelly cystoscope or endoscope of a diameter of 13.0, 14.5, and 16.0 mm. and a length of 40, 46, and 60 mm., respectively, is used by Hartman. Illumination is by a light passed in on a stalk, rather than one fast to the inside of the tube. A head mirror may be used instead. The handicap connected with the tubular forms is lack of ability to distend the upper fornices, where the vagina broadens. In order to provide an inexpensive bivalve I had the double blade used by Harvey Cushing in the nose cut off at 40 cm. on the posterior blade and 35 cm. on the anterior. A lateral handle would be better to guard against soiling by fecal extrusion. Preliminary emptying of the bowel by a finger in the vagina might prevent the nuisance of defecation during inspection, while emptiness of rectum will facilitate spread of the blades of the speculum.

In conclusion, we repeat that the rhesus monkey presents in its cervix so many aspects corresponding to like findings in women in the way of development, injury and inflammation, that it should constitute a valuable experimental animal, particularly if it can be infected with the gonococcus. The rugose cervix seen in a certain proportion of this and other simians is a rather rare find in women.

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DISCUSSION

DR. J. C. LITZENBERG, MINNEAPOLIS, MINN.—When I reported a young ovum between twenty and twenty-four days of age, we had to go to monkey embryology because human material available was inadequate for the necessary comparisons of embryos of different ages. We did find in the monkey, through conference with

Dr. Hartmann, an analogue to our human ovary. The work of Hartmann in endocrinology and ovulation and various other phases and studies in the monkeys, and their similarities to the human being, is familiar to all of you. But they have not been simply scientific studies; they have been attempts to take leaves from the discoveries in the monkey for application in women.

Dickinson's paper does the same thing, for what he has given us today is not simply comparative anatomy. He has made one suggestion, for example, that if this monkey can be infected with gonorrhea, we may learn some things that we do not know about gonorrhea in women. His calling attention to the fact that in the monkey we may do experimental work that we cannot do in women is thus of importance.

Animal experimentation is necessary in order to find out certain biologic and clinical facts, but we have always had to meet the objection that the findings in the white rat, in the mouse, and in the rabbit, may not be the same as in women. With this additional evidence which Dickinson has brought out we may have an animal which is so much nearer to the reactions of woman than any other animal, we may study problems hitherto impossible.

DR. RAYMOND SQUIER, NEW YORK, N. Y.—It is interesting to me that the monkey, which so closely parallels woman anatomically and physiologically, differs so much from her in certain biologic respects. There is some subtle chemical difference that makes the monkey practically refractive to such an organism as the gonococcus, which is infectious for woman. Therefore the monkey cannot be used in the study of gonococcal infections. Of course, this may well be a blessing, for otherwise great damage might be done to experimental colonies.

How deplorable it is also that women do not show the same ease of cervical dilatation during labor as monkeys do, in which animals, so far as I know, the clinical entity of cervical dystocia has not been encountered.

DR. FRED J. TAUSSIG, ST. LOUIS, MO.—There is opportunity for a great deal of valuable scientific work in the field of comparative pathology. Much work has been done on comparative anatomy but very little thus far on comparative pathology. Through it we might very well gain information on such subjects as the blighted ovum, the origin of the amniotic fluid, or the cause of the onset of labor.

DR. OTTO H. SCHWARZ, ST. LOUIS, MO.—I should like to ask Dickinson whether he has any information concerning the presence of myomas in the rhesus monkey. I have asked several veterinarians about this and they seem to have no information at all in regard to it.

DR. EDWARD A. SCHUMANN, PHILADELPHIA, PA.—If Dr. Schwarz will consult a very valuable work, which has small circulation but which is most interesting, he will find an answer to his question. It is called *Diseases in Wild Animals*, by Herbert Fox, a pathologist at the Zoological Gardens in Philadelphia. Myomas have been found and examined in the orang-utan and the rhesus monkey. There has been very little work done in comparative pathology, but this volume has a mine of information which is worth the reading of every student of pathology.

OBSERVATIONS UPON OVULATION IN PRIMATES*

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STATEMENTS with respect to an equal or an alternating ovulatory activity, a subject in which my associate, Dr. G. van Wageningen, and I have recently been interested, appear infrequently in gynecologic literature. Indeed we have met but two references with respect to this problem in women. The first occurs in the article by Fraenkel upon the physiology of the sex organs which is included in the *Handbook* of Halban and Seitz. This author indicates that in general the ovaries in women function alternately, not however in regular turns, but depending upon conditions which are as yet not understood.

The second and much more informative reference is that of Dickinson who, by repeated pelvic examinations, determined that both ovaries swell and become tender to pressure at the midmonth. These changes, however, do not affect both organs equally and in six instances, one ovary was found to be twice the size of the other. In another case in which alternation in activity occurred, the left ovary was enlarged at the time of two expected menstruations and the right once. Twice there was absence of palpable ovarian enlargement or tenderness, and possible absence of ovulation.

Although the observations just mentioned are limited, definite information is available with respect to an alternation of ovulatory function in certain of the lower animals.

Thus Edgar Allen observed that of 21 mice in which data were available for the number of ova produced at 2, 3, and sometimes 4 estrous periods, 4 showed marked and 2 slight alternation of function, while in the others the function was quite evenly divided. Mandl in his series of experiments upon rabbits encountered rarely, instances in which unilateral ovulation occurred. Fraenkel found 11 similar instances in an examination of 272 rabbits. Corner counted 131 fresh corpora lutea in the left and 89 in the right ovaries of 26 sows. The extremes were: left 10, right 0, left 3, right 0, left 2, right 6. Küpfer found that in cows both ovaries function regularly, but that the succession of ovulation is neither routine nor reciprocal. The ovulatory function in this species differs with each animal; sometimes one, sometimes the other ovary functions, although in general the right tends to be more active than the left.

With respect to primates, the largest number of observations upon the alternation of ovulation with which we are familiar are those of Hartman upon monkeys.

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

This author who conducted his investigation by rectal palpation or by laparotomy found that the ovulatory function does not necessarily alternate with regularity between the ovaries, but may involve the same ovary two or three times in succession. Table I taken from Hartman's paper details the findings in his animals. Of a total of 54 ovulations, 27 occurred from the right and 27 from the left ovary.

TABLE I. HARTMAN'S OBSERVATIONS, SUCCESSION OF OVULATORY FUNCTION

(r = right ovary; l = left ovary; - = no observation)

NO. OF ANIMAL	SUCCESSION	HOW DETERMINED
2	l, l, r, r, r, l, r, l	palp.
4	l, r, -, r, l	lap.
7	l, r	palp.
12	r, l	palp.
17	l (?), r (?), l, r	lap.
28	r, r, -, l, r, l, r	lap.
34	l, r	palp.
39	r, l	lap.
39	r, l, r, l	palp.
40	r, r, l, l	lap.
41	r, l, l	palp. and lap.
43	r, r	lap.
45	l, l, r, r, r, l	sections
63	r, l, r, l	lap.
64	r, l, r, l, l	palp.
69	l, r	lap.
79	r, r	lap.
79	l, r, l	lap. and palp.
99	l, r, l	palp.

Since this observation of Hartman is, as far as we know, the only one in which a series of cycles was followed in primates, it occurred to us that an additional report on this point as a part of our investigative project carried out upon the *Macacus rhesus* monkey might prove of interest. In our investigations of the ovulatory activity, we chose the direct method of observation by repeated laparotomies because we had other points in mind which could be determined only by direct visual examination of the ovary in situ. The present paper is concerned primarily with the ovarian findings in the animals in question.

In the present study 8 animals were employed, 6 of which were observed over a period of from thirteen to seventeen cycles. In 2 animals the observations were limited to 4 cycles in the first and to 7 cycles in the second. Including all 8 animals, a total of 94 cycles was studied. As a preliminary measure in order to determine that preoperative menstruation was normal, the animals were observed over a period of three months before the investigation was begun. They were then subjected to laparotomy between the thirteenth and sixteenth days, and the site of ovulation was determined by the presence of a fresh corpus luteum in the individual ovary. Nembutal proved a satisfactory anesthetic and strict surgical technique was employed. This and the care exercised by Dr. van Wageningen, who did the major number of the laparotomies, resulted in the formation of remarkably few postoperative adhesions. Except-

ing the skin suture of fine black silk, the abdominal wound was approximated with sutures of fine catgut. As can be seen from Table II the slight operative procedure which we employed had no effect upon the occurrence of the subsequent menstrual cycles.

In all, 94 laparotomies were performed during the corresponding cycles, and the presence or absence of a fresh corpus luteum determined. Eighty-six of these cycles were associated with ovulation, while in 8, menstruation was nonovulatory in character. Of the total number of menstrual cycles associated with the presence of a corpus luteum, the structure was present 52 times in the right and 34 times in the left ovary. The character of sequence or of alternation of ovulation in the individual animals is shown in Table II.

TABLE II. SUCCESSION OF OVULATORY FUNCTION

r = right ovary 0 = no ovulation
l = left ovary - = no observation

NO. OF ANIMAL	SUCCESSION	SUMMATION
M.m. 160	l, l, r, l, r, l, l, r, r, 0, -, r, 0, r, r	7 right, 5 left ovary 2 nonovulatory cycles
M.m. 188	r, l, r, r, r, r, -, r, 0, l, r, l, l, r, r	9 right, 4 left ovary 1 nonovulatory cycle
M.m. 189	l, r, r, 0, sick	
M.m. 191	r, r, l, -, r, r, l, l, -, r, l, l, r, l, r, l	8 right, 7 left ovary 0 nonovulatory cycles
M.m. 192	r, l, r, r, l, r, l, -, l, r, l, l, r, r, l, l, r, r	9 right, 8 left ovary 0 nonovulatory cycles
M.m. 193	l, r, r, l, -, -, r, l, r, r, l, l, r, l, l, 0	6 right, 7 left ovary 1 nonovulatory cycle
M.m. 195	r, l, r, l, 0, 0, -, -, r, r, r, 0, 0, r, r	7 right, 2 left ovary 4 nonovulatory cycles
M.m. 196	r, r, r, l, r, r, r, sick	6 right, 1 left ovary 0 nonovulatory cycles

The results of these observations are similar to those of Hartman quoted above, and in the first place confirm his observations that in the *Macacus rhesus* although the ovaries, as in other animals, must be subjected to the same hormonal influences, there is no rule for the sequence or for the alternation of ovulatory function. Indeed as was shown in one animal, Monkey 196, in which of a total of 7 observations the corpus luteum was found upon the right side in six, ovulatory activity may be confined to one ovary although the other organ is present and, as far as can be determined anatomically normal.

In this connection the findings of G. van Wagenen with respect to the incidence of ovulation in the monkey from which one ovary had been excised is of interest. In three of Dr. van Wagenen's unilaterally gonadectomized macaques, exploratory laparotomies showed that ovulation had taken place in 14 out of 20 cycles. The ovary was examined from the seventeenth to the twentieth day of the cycle and the presence of a newly ruptured follicle or a corpus luteum of good size and healthy ap-

pearance was taken as evidence of ovulation. The remains of the previous corpus luteum could always be seen in the expected position in the ovary.

Eight consecutive cycles were studied in two monkeys and four in the third. The first six observations were positive in one animal; the first four and the first three in the other two animals. In two animals bleeding from the uterus began on the third day following a laparotomy, giving short cycles of nineteen and twenty-one days. Ovulation did not occur in cycles initiated by these early bleedings. One ovulation was recorded without any observed menstruation.

In the second place the observation first emphasized by Corner in his study of ovulation and menstruation in *Macacus rhesus* and subsequently pointed out by others, that menstruation in the monkey may occur in the absence of ovulation, is again confirmed by our own work. With respect to this point Edgar Allen states that even in primates the hormone of the corpus luteum is not necessary for menstruation, for the follicles need not develop to the point of ovulation, and in monkeys usually do not during the spring and summer of the year. Successive periods of menstruation may occur during these nonovulating seasons and these menstrual periods are, as we have also noted, indistinguishable externally at least from those which occur during the mating season when ovulation is the rule. In addition, Allen has noted that in menstrual cycles without ovulation, the endometrium and mammary glands do not undergo the full premenstrual transformation, although the typical changes of edema in the subepithelial connective tissue and the extravasation of blood which immediately precedes the menstrual hemorrhage is present.

Novak has emphasized the possibility of human menstruation without ovulation, the periodic bleeding being indistinguishable from normal menstruation though at times there is some irregularity and some excess above the usual loss of blood. In his opinion a study of the endometrium will show, if ovulation has occurred, the characteristic secretory changes dependent upon the presence of the corpus luteum hormone. If, on the other hand, there is a complete absence of secretory changes, it may be assumed that ovulation has not occurred. The similarity of the histologic picture in the endometrium from such patients, to that found in monkeys in which it is known that menstrual bleeding has taken place in the absence of ovulation, would seem to support Novak's contention. Moreover, if, as Edgar Allen suggests, an insufficiency of the anterior pituitary gonad stimulating hormone may explain the frequent anovulatory menstrual cycle of monkeys a similar insufficiency may account for similar cycles in the human being.

Finally, in connection with the general question of the time and occurrence of ovulation a recent study made by Burr, Hill, and Allen is

pertinent. Burr and his associates have developed a vacuum tube potentiometer which is stable, draws almost no current from the living system and is independent of interelectrode resistance up to one megohm. With this instrument it is possible to record accurately minute voltage changes in living systems under a wide variety of circumstances.

Applying the apparatus to a study of ovulation in rabbits, it was found that readings taken previous to the eighth hour after mating, established a fairly uniform base line. Subsequently a distinct but gradual rise from the base line occurred. In the first rabbit as the ninth hour after mating approached, a sharp rise of potential occurred which was 45 times greater than the control variation. Twelve minutes later a similar change in potential was repeated. A third rise and fall occurred seventeen minutes after the second surge. Following these records an examination of the ovaries at laparotomy showed 3 rupture points, 2 in one ovary and 1 in the other. A comparison of the recordings obtained from other animals with their ovaries at laparotomy showed that in each animal the number of rises in potential equalled the number of ruptured follicles. As the authors indicate, these findings suggest that with the aid of this new instrument, it is possible to determine with great certainty in the intact animal the time and duration of ovulation, the instant of follicular rupture and the exact number of ovulations. While a study of ovulation in the human being has as yet not been carried out with this instrument, the results obtained suggest that similar results may be found in woman. If this proves to be the case there will be at hand an additional means for study, which should yield further information respecting the alternation of ovulatory function and anovulatory menstruation in woman.

To recapitulate, the present paper details the results of a study by repeated laparotomy of the alternation of ovulation in the *Macacus rhesus* monkey. In addition, it speaks briefly of the problem of anovulatory menstruation and of the recent method for the detection of ovulation devised by Burr, Hill and Allen.

We wish to acknowledge our indebtedness for assistance to our laboratory technicians, Miss Ruth Vogel and Mr. Joseph Negri. The study was subsidized by a grant from the Research Fund of the School of Medicine.

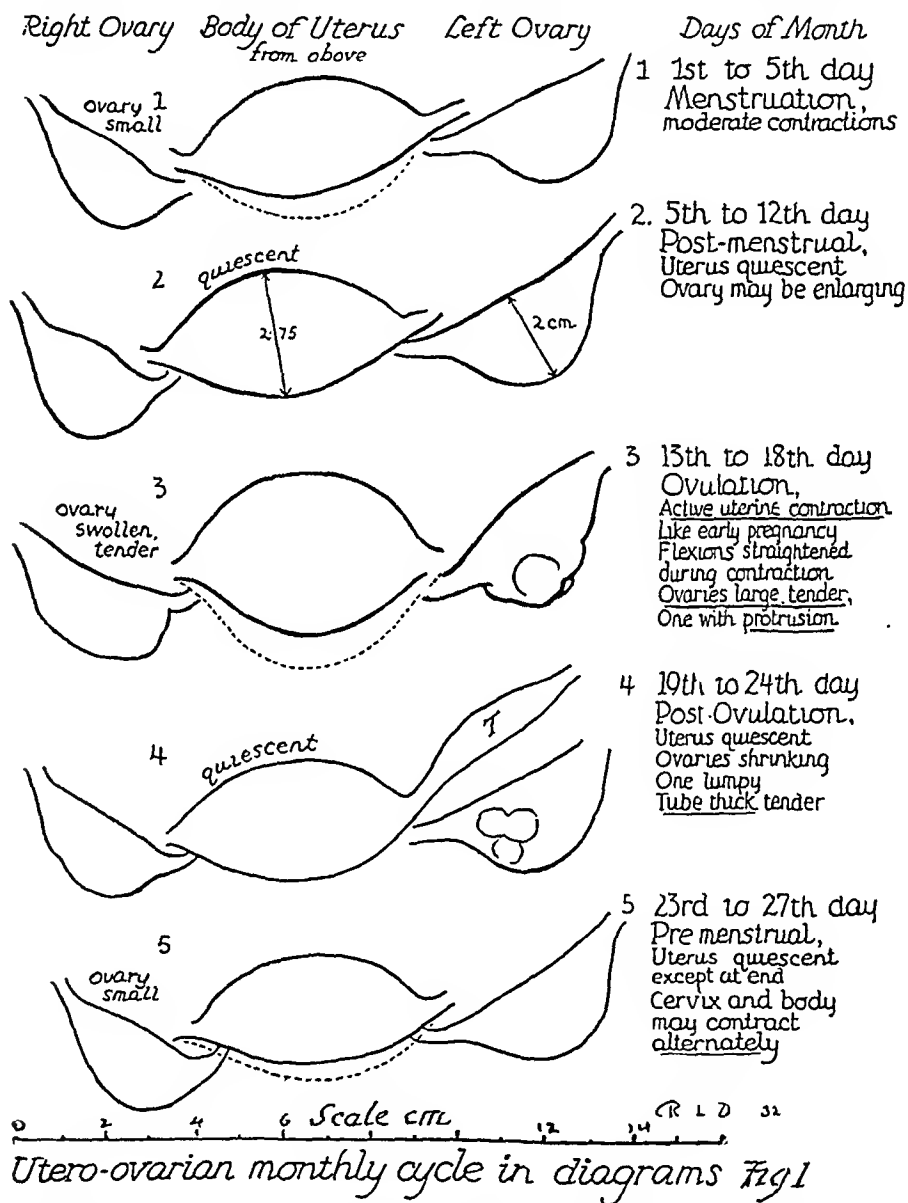
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DISCUSSION

DR. ROBERT L. DICKINSON, NEW YORK, N. Y.—The time of ovulation may be profitably studied in women by bimanual palpation, but from my experience with both, it is vastly more difficult than in small monkeys. With patients with relaxed abdominal wall, one or both ovaries may be caught and outlined, the right against

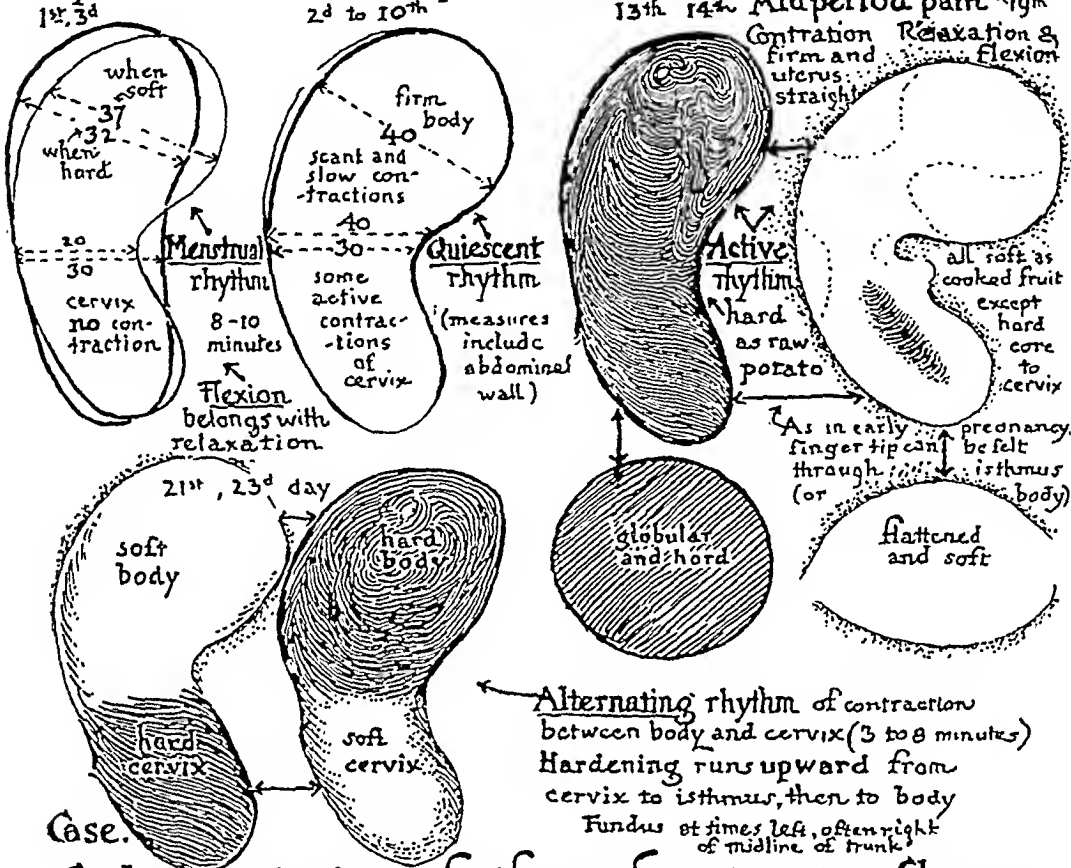


the lateral pelvic wall, the left between the fingertips of the outer and inner hand. Thus the enlarged follicle or the corpus luteum can be detected. An easier procedure is the seizure of the body of the uterus and the recognition of definite contraction and relaxation in its rhythmic activity, which is pronounced during the days of maximum distention of the follicle in many women.

Any procedure which would date ovulation in a given individual would help in the selection of times for desired conception, and safety from conception. Examina-

tions would only be needed to find the time of active contractions, and they are superfluous when ovulation is indicated by pelvic ache, by ovarian tenderness, or self-palpation or by breast ache. Five patients were examined at two- or three-day intervals for three months, at the same time of day, with empty bowel, and yielded

Days of menstrual cycle



Case.

Cycles in uterine rhythms of contraction: Change in size, form and tenderness in ovary (& tube)

On right side, day of cycle

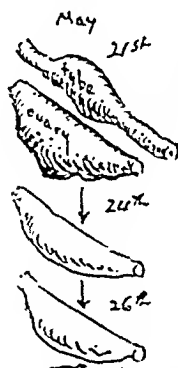
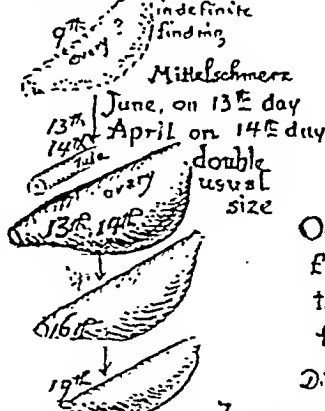


Fig 2: Scale

right side



left side



Case No

S 1150

sketches

on history

1932

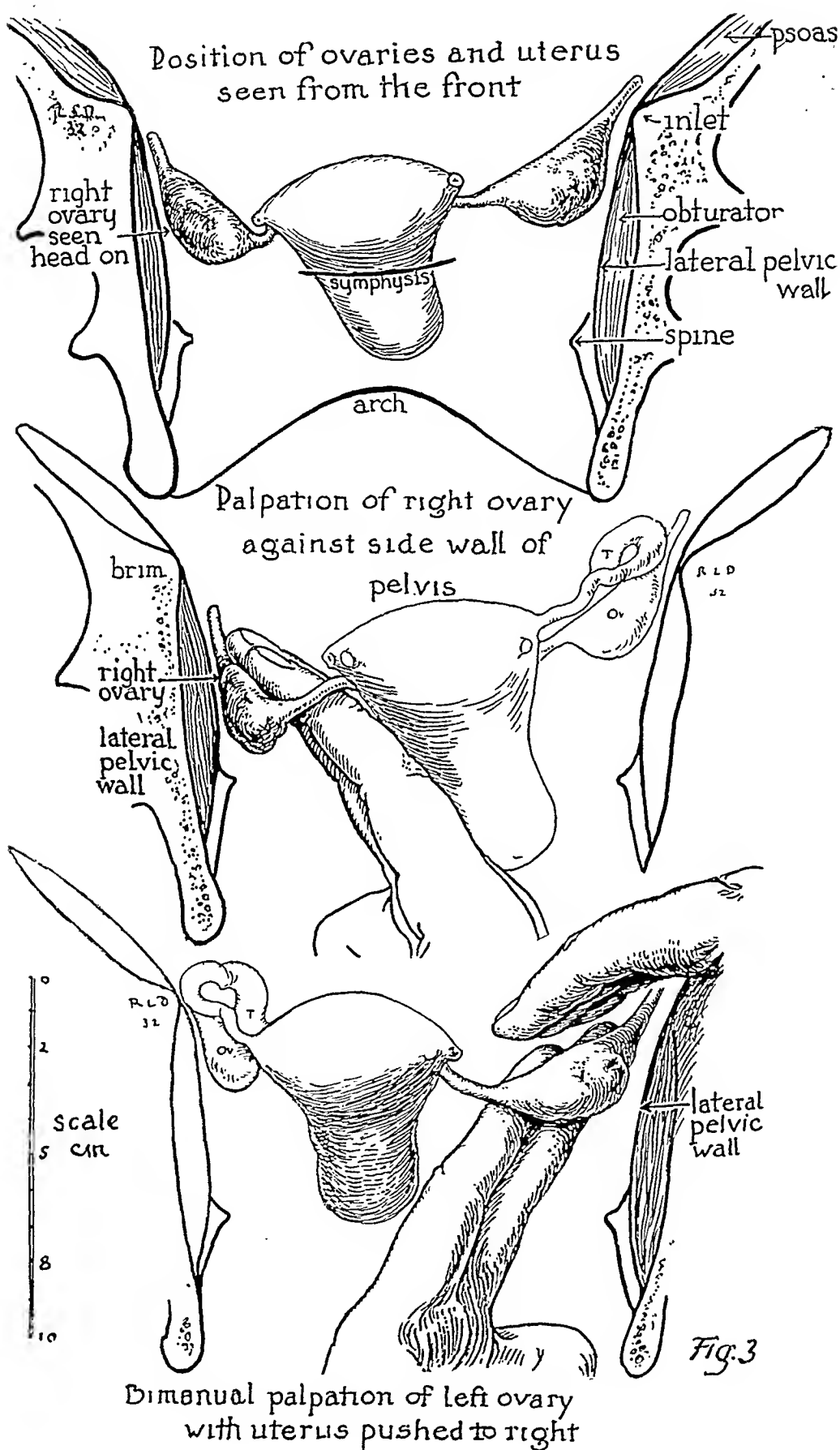
Ovulation first, left; then right; then left

Dickinson 1932

89 observations. In addition, some records of Mittelschmerz were examined, and my early publications were drawn upon. These data point to the following conclusions:

1. The uterus in the nonpregnant exhibits steadily recurring rhythmic contractions and relaxations.

2. The intervals range from two to twenty minutes, as found by palpation.



3. These contractions fall into three main periods, one of major activity at or about the time of ovarian enlargement, preceded and followed by periods of relative quiescence.

4. Before and during menstruation a minor increase in frequency and excitability may be found.

5. In examining the uterus during ovulation, the findings suggest early pregnancy as do also the vacillations in the size and compressibility of various segments found while palpating.

6. Both ovaries enlarge and become tender, and one may have a protruding mass, while later the corresponding tube may swell.

7. During contraction any flexion (normal or otherwise) partially straightens out.

8. Corpus and cervix may alternate in rhythm.

9. A wave of contraction may be found starting in the cervix, passing to the isthmus, and thence to the corpus. Except in isolated isthmus relaxation (Hegar's sign) the isthmus usually acts with the corpus.

Both ovaries swell and become tender to pressure at the midmonth, but one more so than the other, in six instances one being recorded as "twice the size of the opposite ovary." On the larger ovary a protruding mass may be found. A couple of days later, with lessened size and tension, a nodular feel like a "blackberry" has been noted.

One ovary may do more than its share, the left seeming to be the more active, both in palpated patients and from my "Mittelschmerz" reports. With midperiod pain both sides usually ache or are tender to the patient's pressure on the lower abdomen, but when asked to record the relative degree of tenderness or pain between one ovary and its fellow, several patients report alternation between one month and the next. In one case personally studied three months' alternation in activity occurred, the left ovary being enlarged twice at the expected time, and the right once, but three days late. Twice there was absence of palpable ovarian enlargement or tenderness at the midmonth, suggesting a possible absence of ovulation.

Tubal thickening and tenderness have been observed a few days after the supposed date of ovulation, on the side of the affected ovary, in four instances.

The patient seemed to adhere to a given time in the cycle within three days, in the five palpated and in six midpain patients. In one case the findings of three periods pointed to the thirteenth, fourteenth, and seventeenth day, respectively. Yet one palpated patient showed uterine changes on the ninth day once, on the sixteenth day once, and the findings were uncertain once.

DR. RAYMOND SQUIER, NEW YORK, N. Y. (by invitation).—It seems to me that one interesting direction that research in ovulation will take is toward the quality of the ovum. Whereas the factors responsible for the mechanical release of the egg from the ovary are coming to be increasingly well known, what develops the ovum itself remains a mystery.

The quality of ova, as Streeter and associates have emphasized, has an important bearing on spontaneous abortion. We know that among laboratory animals as many as one-fifth of ova are sufficiently defective to be so recognized microscopically, as early as the time of ovulation. Further abnormalities show up later, perhaps either preventing implantation or causing subsequent abortion of the conceptus at any stage of gestation.

The existence of nonovulatory menstrual cycles in the monkey, especially during the summer in this latitude, has been well established by Hartman and Corner, and there is accumulating clinical evidence that they occur in women.

These two lines of interest may some day converge for the answer to this interesting question: Just as there are variations, seasonal or other, in the incidence of ovulation, may there not be also variations, parallel or independent thereof, in the incidence of defective ova? Such variation might be reflected as temporary sterility or as spontaneous abortion.

THE SIZE AND SHAPE OF THE PELVIC INLET AS DETERMINED BY DIRECT MEASUREMENT*

EDWARD A. SCHUMANN, A.B., M.D., F.A.C.S., PHILADELPHIA, PA.

THE work of Caldwell and Moloy, Thoms, Jarcho and others has again drawn the attention of obstetricians to the architecture of the pelvis. In view of the various opinions expressed as to the size and shape of the pelvic inlet, it was determined to measure a series of pelves directly through the abdominal incision, in patients subjected to laparotomy, for various gynecologic lesions. Accordingly, a number of pelves were so measured at the Kensington Hospital for Women, the technic being to determine the length of the anteroposterior and greatest transverse diameter of the inlet, with a De Lee outlet pelvimeter. This was easily accomplished by inserting the instrument through the abdominal incision and then, while the operator controlled the position of the tips to insure their being correctly placed, the assistant spread the handles of the pelvimeter and read the scale. These measurements were carried out during the course of abdominal operations and the patients were not selected, but taken consecutively. During the period of convalescence, careful external pelvimetry was performed on all these women, and their obstetric histories, if any, were obtained, the results being correlated as shown in Tables I to IV.

As a result of this investigation, certain definite conclusions were drawn. First, that the oval inlet is more common than any other type, 40 per cent of our cases possessing such oval pelves of ample size, while another 26 per cent presented oval pelves of the flat type. Next in order were the round pelvic inlets, which accounted for 24 per cent, and still less frequent was the anthropoid type, which was found in 10 per cent of the cases studied.

A considerable series of patients was investigated but, inasmuch as there was no variation in the occurrence of the different types, only the first fifty cases are here analyzed in detail.

In the oval pelves of large size the anteroposterior diameter varied from 10.5 cm. to 12.25 cm., the average being 11 cm. The transverse varied from 12 cm. to 13 cm., the average being 12.25 cm. It is interest-

*Read at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

ing to note that the largest pelvis measured belonged to this group, its diameter being 12.25 by 14 cm., the patient having a double uterus but having never been pregnant. Of the small and flat oval pelves, the anteroposterior diameter varied from 9.5 to 10.5 cm., the average being

TABLE I. OVAL PELVES, LARGE

CASE	MEASUREMENT OF INLET		EXTERNAL PELVIMETRY				OBSTETRIC HISTORY	
	A. P.	TR.	I. S.	I. C.	TROCH.	EX. CON.	NUMBER OF CHILDREN	WEIGHT POUNDS
2	10.5	× 12.5	24.5	28.0	29.0	19.0	1	7
4	11.0	× 12.5	27.5	31.0	32.5	20.5	2	7½-8½
9	10.75	× 12.0	27.0	29.0	34.0	20.0	1	8
10	11.25	× 12.5	25.0	27.5	32.0	22.0	1	7½
12	11.0	× 12.25	27.0	30.0	34.0	22.0	4	Full size
14	11.25	× 12.75	25.0	28.0	31.0	19.5	None	
15	10.75	× 12.0	24.0	26.0	29.5	18.0	None	
21	10.75	× 12.75	27.0	30.0	34.0	20.5	2	7-13
23	11.0	× 13.0	26.0	29.0	32.5	19.5	1	6½
24	11.5	× 12.25	27.0	30.0	32.0	22.0	1	9½
27	11.75	× 12.5	25.0	28.0	31.0	20.0	None	
32	11.0	× 11.5	27.0	29.0	33.5	20.0	1	7
36	11.5	× 12.25	28.0	30.0	31.0	20.0	1	6
38	11.0	× 13.0	25.0	27.0	30.0	19.0	None	
40	11.25	× 12.25	25.0	29.0	32.0	20.0	3	7-6-8
43	12.25	× 14.0	31.0	32.0	37.0	20.0	None	
50	12.5	× 13.0	28.0	31.0	33.5	21.5	(double uterus) 1	8
31	11.25	× 12.0	26.0	27.0	32.0	18.5	4	8½-8-7-7½
42	10.5	× 12.5	27.0	29.0	33.0	18.5	11	All spon.
44	10.5	× 11.0	25.0	27.0	31.0	20.0	None	

TABLE II. OVAL PELVES, SMALL; ALSO FLAT TYPE

CASE	MEASUREMENT OF INLET		EXTERNAL PELVIMETRY				OBSTETRIC HISTORY	
	A. P.	TR.	I. S.	I. C.	TROCH.	EX. CON.	NUMBER OF CHILDREN	WEIGHT POUNDS
5	10.0	× 11.0	22.0	25.0	28.0	18.5	2	6-6½
6	10.5	× 12.5	23.0	26.0	29.0	17.5	1 (forceps)	8
7	10.5	× 13.0	24.0	28.0	30.0	19.0	4	10-10-9½
8	9.5	× 12.0	30.0	31.0	22.0	7.0	1 (forceps)	7
16	10.0	× 12.0	24.0	26.5	31.0	20.0	8	Unknown
19	10.0	× 12.25	26.5	29.75	30.25	19.0	None	
20	9.75	× 11.0	27.0	28.5	32.0	17.5	2 (both forceps)	4-4
25	10.25	× 13.5	27.0	30.0	32.0	22.0	4	6-7-7-8
28	9.5	× 11.0	26.5	27.5	32.0	20.0	3	8-7-4½
34	10.0	× 11.5	25.0	28.0	32.0	20.5	1	7
35	9.0	× 13.0	26.0	27.0	30.0	22.0	7 (1 forceps)	Children all large.
46	10.0	× 12.0	25.5	27.5	31.0	17.0	1	7
48	10.0	× 12.0	24.0	27.0	28.5	18.5	None	

10 cm., while the transverse on the average was 12. The round pelves averaged 11.5 by 11.5 cm. Another interesting point is that, although 38 of the 50 patients examined had borne one or more children, none of them had had any particular obstetric difficulties, and only six had required instrumental deliveries.

In no patient was any marked pelvic contraction observed. The external pelvimetry, which was carefully performed in all of these patients, is noteworthy by the fact that the figures so obtained bear little or no relation to the actual size of the pelvic inlet. This is true of all the external diameters but particularly impressive in the external conjugate, which varied within wide limits from the true conjugate.

It would seem that external pelvimetry must be more and more disregarded as a means of obstetric diagnosis, because the gross errors

TABLE III. ROUND INLETS

CASE	MEASUREMENT OF INLET		EXTERNAL PELVIMETRY				OBSTETRIC HISTORY	
	A. P.	TR.	I. S.	I. C.	TROCH.	EX. CON.	NUMBER OF CHILDREN	WEIGHT POUNDS
1	12.25	12.25	26.5	29.5	33.0	20.5	None	
11	12.5	12.5	29.0	33.0	35.0	21.0	3	8-8-9 spon.
17	11.0	11.0	27.0	29.0	33.0	20.0	3	8-9-8½ spon.
18	11.5	11.5	24.5	27.1	30.0	19.5	None	
26	11.5	11.5	25.0	29.0	30.0	21.0	1 (forceps long labor)	Weight not known
29	12.25	12.5	27.0	30.0	33.0	21.0	3	8-6-9 spon.
41	11.5	11.5	26.0	28.0	31.5	19.5	None	
45	11.25	11.5	25.5	28.0	33.0	21.0	2	7-11
47	11.5	11.5	26.5	29.0	33.5	21.0	2	7-4
49	11.5	11.5	24.0	26.5	29.0	18.0	2	5-4
3	12.0	12.5	25.5	27.5	31.0	19.0	None	
13	12.0	12.5	25.0	29.0	33.0	21.0	None	

TABLE IV. ANTHROPOID PELVIS

CASE	MEASUREMENT OF INLET		EXTERNAL PELVIMETRY				OBSTETRIC HISTORY	
	A. P.	TR.	I. S.	I. C.	TROCH.	EX. CON.	NUMBER OF CHILDREN	WEIGHT POUNDS
22	13.0	12.25	24.5	26.5	33.0	22.0	2	10-7
30	13.0	11.5	25.0	28.0	31.5	20.5	2	6 prenat.
33	12.5	11.5	28.0	31.0	33.0	23.0	6	Average size
37	11.5	11.0	22.5	26.0	30.0	18.0	None	
39	12.0	11.5	27.0	29.0	33.0	21.0	3	6½-6-9

involved in it may well lead the inexperienced obstetrician into a false sense of security, when in point of fact, severe pelvic contraction may exist.

In order to determine the accuracy of roentgenologic measurement of the pelvis, a group of the foregoing patients were subjected to measurement by the technique of Thoms, and it was extremely gratifying to learn that the diameters of the inlet as determined by direct intra-abdominal measurement corresponded in every instance with those obtained by this technique, the variation being constantly less than 2 mm.

The conclusions reached from this investigation are:

1. That the oval pelvis is much the most frequent type met, followed in order by the round and the anthropoid forms.

2. That external pelvic measurements are unreliable as indicators of the true size of the inlet.

3. And last, that the technic of Thoms may be relied upon as an accurate method of evaluating pelvic size and shape.

1814 SPRUCE STREET

DISCUSSION

DR. ALFRED C. BECK, BROOKLYN, N. Y.—This method of direct measurement of the pelvic inlet is simple and apparently very accurate. It should be useful to those of us who do both obstetrics and gynecology. We now can easily measure the inlet of those women in the reproductive period who are subjected to laparotomy. Its use ought to be particularly indicated in the nulliparous woman and in those who have had trouble in a previous labor.

I was pleased to hear Dr. Schumann state that he also found that external pelvimetry is unreliable, but that this method, when used to check the work of Dr. Thoms, indicated that his x-ray observations were very accurate. I believe that Dr. Thoms' x-ray observations are among the significant contributions made to obstetrics in our time.

*(American Gynecological Society*papers to be concluded in the December issue.)*

THE INVESTIGATION OF A NEW PENTAVALENT ARSENICAL, ALDARSONE, IN THE TREATMENT OF TRICHOMONAS VAGINITIS*

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A SURVEY of the recent literature indicates that the treatment of trichomonas vaginitis by drying plus antisepsis has largely replaced the use of liquid antiseptics.

The technic for the dry antiseptic treatment consists generally of a preliminary washing of the vagina and external genitalia by some mild liquid antiseptic or cleansing agent, drying, followed by the application of the active drug in the form of a powder, tablet, paste or ointment. Many chemotherapeutic agents have been thus employed as trichomonadicidal drugs, including Lassar's paste,²⁰ zinc oxide ointment,²¹ kaolin,³ cornstarch,¹⁹ metaphen ointment,⁶ quinine sulphate,¹⁷ salicylic acid,¹² sodium bicarbonate,² and acetarsone.¹³

The excellent results of treatment of various protozoan diseases by organic arsenicals prompted the usage of acetarsone, in the form of tablets and powder mixtures for the dry treatment of vaginal trichomoniasis.

*The laboratory investigation of aldarsone was aided by a grant from the Abbott Laboratories, North Chicago, Ill.

Laboratory investigation of aldarson (preparation No. 1,717), a soluble pentavalent organic arsenical chemically related to acetarson, which has recently been synthesized and described by Raiziss, Severac and Kremens,²² led to the discovery that this compound* has many times the trichomonadocidal power of acetarson, is less toxic, and has the additional advantage of being highly hygroscopic.

In view of these laboratory findings an extensive series of clinical observations were also undertaken to evaluate the efficacy of aldarson in the treatment of vaginal trichomoniasis. Similar studies with acetarson were conducted simultaneously in order to afford an adequate basis of comparison.

MATERIALS AND METHODS

Experiments in vitro.—The trichomonadocidal power of aldarson and acetarson were determined by the following method.

Various concentrations of the drugs in distilled water were prepared. In the case of aldarson, clear pale yellow solutions were obtained, while acetarson yielded heavy white suspensions. Solutions of acetarson were prepared by adding sufficient sodium bicarbonate to dissolve the arsenical.

One-half cubic centimeter of the preparation to be tested was mixed in a small test tube with an equal quantity of a heavy suspension of freshly collected vaginal material in Ringer's solution, containing numerous active trichomonads. The final concentration of the drug was therefore one-half that of the original preparation.

At the instant of contact of the drug with the organisms a stop watch was started. After a few seconds of vigorous mixing a drop of the mixture was placed on a glass slip and observed under the microscope, first with the low power lens and then more minutely with the high dry objective. The time was recorded when total cessation of movement had occurred in all the organisms. Since the flagella and undulating membrane may continue slow rhythmic motion for some time after actual displacement of the organism has ceased, these structures must be carefully focused upon.

If death of the organisms did not occur within a few minutes, observation was continued upon a fresh drop. Each observation was repeated three times and an average was taken.

To note the influence of additional organic material upon the trichomonadocidal power of the drug, experiments were also performed with solutions and suspensions of the drugs in human blood serum.

CLINICAL STUDIES

A total of 135 patients in attendance at the antenatal and postnatal clinics of the Department of Obstetrics, Jefferson Medical College Hospital, Philadelphia, were treated for trichomonas vaginitis. Ninety-six were pregnant women in the first, second, or early weeks of the third trimester of gestation, while 39 were nongravid patients. The patients selected exhibited clinical and microscopic evidence of infestation with *Trichomonas vaginalis*.

One hundred women were treated with aldarson, 25 received treatment with acetarson, while in 10 patients used as control subjects, kaolin alone was used.

*This drug was prepared and supplied for this study by the Dermatological Research Laboratories, Philadelphia, Division of Abbott Laboratories, North Chicago, Ill.

The following technic was employed in the treatment of these women:

With the patient in the lithotomy position, the vagina was exposed with a bivalve speculum and the mucosa thoroughly washed with a diluted tincture of green soap and water. The vaginal membrane was then thoroughly dried with cotton pledgets.

The vaginal portion of the cervix was painted with tincture of metaphen, and a number of applicators dipped in the solution were successively carried deep into the cervical canal.

The introitus and vulva were thoroughly scrubbed with tincture of green soap and water, and then dried.

The urethra and paraurethral recesses were treated with an aqueous solution of metaphen 1:500, repeatedly applied on cotton applicators.

The antiseptic powder preparation was insufflated into the vagina with a powder blower. One-half gram of the arsenical with finely divided kaolin sufficient to make 3 gm. was used for each treatment. A number of vaginal insufflators were successfully used, including the Gellhorn powder blower,¹³ the Powdex insufflator, the Shelanski insufflator, and several designed by Dr. G. W. Raiziss.

The patient was treated in this manner on three consecutive days. Three additional treatments were given at three-day intervals. The patient was instructed not to douche and to refrain from intercourse during the period of treatment.

A microscopic research for trichomonads was made before each treatment and at regular intervals thereafter. Smears from the vagina and cervix were taken to note changes in the bacterial flora.

In a number of instances, because of failure of cooperation on the part of the patients, completion of the series of treatments or posttreatment check-ups was not possible. The records of such patients were withdrawn from the study and replaced by others.

RESULTS

Studies in vitro.—The killing time of solutions of aldarson of a number of concentrations for *Trichomonas vaginalis* are given in Table I. The range among the ten strains of trichomonads tested, as well as the calculated average killing time is given.

TABLE I. RESULTS OF EXPOSURE OF TEN STRAINS OF TRICHOMONAS VAGINALIS TO ALDARSONE AND ACETARSONE (MICROSCOPIC EXAMINATION)

DRUG	FINAL CONCENTRATION OF DRUG IN TEST MIXTURE	RESULTS	
		AVERAGE KILLING TIME	RANGE
Aldarson	1:10	At once*	-----
	1:20	20"	At once to 90"
	1:30	4' 40"	4' 15" to 7'
	1:40	13' 50"	6' to 22' 30"
Acetarson	Saturated Solution	Actively motile after 1 hour	
	1:20 Suspension	Slowly motile or "rounded up" with flagella still beating, after 1 hour	
	1:20 Solution (Dissolved by addition of NaHCO ₃)	Actively motile after 1 hour	

*Approximately fifteen seconds are required to make an initial observation.

In concentrations of aldarson up to 1:10 all strains were killed at once, that is before they could be observed under the microscope. Aldarson 1:20 had an average killing time of twenty seconds.

Table II reveals that large concentrations of organic material had little effect on the trichomonadocidal power of aldarson. Solutions of aldarson 1:30 in 25 per cent human blood serum and in distilled water were almost equally effective. It will be recalled that considerable quantities of organic material were present in all of the test mixtures, since one-half of the test preparation consisted of a heavy suspension of vaginal secretion in saline.

The results with acetarsone (Table I) indicate a comparatively low trichomonadocidal power.

The ten strains of organisms studied were all actively motile after an exposure of one hour to a saturated solution of acetarsone. In a suspension of acetarsone, in which its final concentration was 1:20, the organisms were either slowly motile or "rounded up" with flagella still beating after an exposure of one hour.

The trichomonadocidal power of a carbonated solution of acetarsone 1:20 was even lower than the suspension, since in every instance the organisms were actively motile after one hour.

TABLE II. EFFECT OF HUMAN BLOOD SERUM ON TRICHOMONADICIDAL POWER OF ALDARSONE

SOLUTION TESTED	FINAL CONCENTRATION OF ALDARSONE IN TEST MIXTURE	AVERAGE KILLING TIME (5 TESTS)
Aldarson 1:15 in 50 per cent human blood serum	1:30*	5' 35"
Aldarson 1:15 in distilled water	1:30	5' 20"

*In the final test mixture the concentration of human blood serum is 25 per cent.

Clinical Results.—The results of treatment of 135 patients with trichomonas vaginitis are given in Tables III and IV, based on the findings at the last periodic examination, three to nine months after treatment.

It is shown in Table III that 84 per cent of 100 patients responded to a series of 6 treatments of aldarson and have since remained microscopically negative. Of the 16 patients who had recurrences, 5 remained negative following 6 additional treatments, and 3 required a total of 18 treatments.

TABLE III. RESULTS OF TREATMENT

	ALDARSONE	ACETARSONE
Total No. of patients treated	100	25
Total No. remaining free from trichomonas	91 or 91%	12 or 44.4%
Required 6 treatments	84 or 84%	7 or 28.0%
Required 12 treatments	5 or 5%	2 or 8%
Required 18 treatments	2 or 2%	2 or 8%
Total No. not cured	9 or 9%	13 or 55.6%

TABLE IV. PERIOD OF OBSERVATION OF PATIENTS TREATED WITH ALDARSONE AND THEIR PRESENT STATUS

PERIOD OF OBSERVATION	NO. OF PATIENTS	PRESENT STATUS	
		NEGATIVE	POSITIVE
9 months	5	5	0
8 months	10	10	0
7 months	19	16	3
6 months	25	22	3
5 months	14	13	1
4 months	16	15	1
3 months	11	10	1
	100	91	9

In 3 nonpregnant women badly eroded cervixes were treated with the electric cautery before the institution of the third series of treatments, with the result that in 2 of these women cures were obtained.

Of the total group of 100, nine are still clinically and microscopically positive.

Permanent disappearance of the trichomonads was invariably accompanied by a disappearance of the leucorrhea. Generally the microscopic appearance of the secretion returned to normal, together with the appearance of the normal bacterial flora. In a few instances the profuse leucorrhea of vaginal trichomoniasis was replaced by a moderate white mucopurulent discharge, resulting from cervical disease.

In Table IV a résumé of the period of time is given during which the patients have been observed together with a tabulation of their present status. It will be noted that 59 patients have been observed for six to nine months, while the remaining 41 have been followed for three to six months.

A comparison of the results obtained among pregnant and nonpregnant patients treated with aldarson is presented in Table V. The end-results for each group are approximately equal, 91.7 per cent of 72 pregnant patients remained negative, compared to 89.3 per cent of 28 nonpregnant women.

Recurrences were tabulated after each series of six treatments. Sixteen recurrences were noted following the first series of treatments with aldarson among 100 patients. A second recurrence was obtained in 11 of the 16 patients, after a second series of treatments. Nine women had a third recurrence following the third group of treatments.

The total of 36 recurrences have been classified in Table VI, with reference to the interval of time which elapsed between the last treatment and the time when the recurrence was noted. More than half of these occurred in the first two weeks of observation, while the remainder were noted at intervals up to eight weeks. No relapses occurred after a period of negativity of eight weeks in patients observed for three to nine months.

TABLE V. COMPARISON OF RESULTS OF TREATMENT WITH ALDARSONE AMONG PREGNANT AND NONPREGNANT PATIENTS

	PREGNANT PATIENTS	NONPREGNANT PATIENTS
Total number treated	72	28
Total number remaining negative	66 or 91.7%	25 or 89.3%
Required 6 treatments	61 or 84.7%	23 or 82.2%
Required 12 treatments	5 or 6.9%	0
Required 18 treatments	0	2 or 7.1%
Total number not cured	6 or 8.3%	3 or 10.7%

TABLE VI. ANALYSIS OF RECURRENCES FOLLOWING TREATMENT WITH ALDARSONE

Following first 6 treatments	16
Following second series of 6 treatments	11
Following third series of 6 treatments	9
	36
During first two weeks	22
Second to fourth week	7
Fourth to sixth week	4
Sixth to eighth week	3
Eighth to thirty-sixth week	0
	36

Of 23 recurrences among pregnant women, only 2 were noted after delivery.

Among the nonpregnant women the recurrences were noted chiefly after the next menstrual period, and occasionally not until the second menstrual period following the treatment.

The results of treatment with acetarsone are given in Table III.

Eleven or 44.4 per cent of 25 patients treated remained negative after a period of observation of six to eight months. Seven of the patients cured remained negative after six treatments, 2 patients required an additional series of treatments, while 2 others remained negative after 2 additional series of treatments. Thirteen or 55.6 per cent of the group remained uncured after a total of 18 treatments with acetarsone.

Seventeen of the women in this group were pregnant, while 8 were nongravidas. The percentage of cures in the pregnant group (50 per cent) was somewhat greater than in the nonpregnant group (41.2 per cent).

Of the 10 control patients one has remained free from *T. vaginalis* after a period of six months, following 6 treatments in which kaolin alone was used for insufflation, after preliminary treatment with tincture of green soap, and the application of metaphen to the cervix and urethra. The other 9 controls received 3 series of 6 treatments, following which recurrences were noted in each instance.

In no instance were toxic symptoms or other reactions following the administration of acetarsone or aldarsone noted, although as many as 18 treatments using a total of 9 gm. of the arsenicals were administered to a number of patients during the course of five weeks.

DISCUSSION

Although many antiseptics have a high trichomonadicidal power in vitro, relatively few are clinically effective. The inability of these drugs to keep the vagina proper free from organisms may be the result of their rapid absorption, their inactivation within the vagina, or the fact that they are diluted and drained away from the vaginal canal.

The good results following the insufflation of antiseptic powders is in large measure the result of the long-continued action of the drug, thus not only destroying organisms with which they come into contact, but also inhibiting reinfestation by those that are not reached. In addition the maintenance of a dry vagina which is favored by powders, is in itself inimical to multiplication of trichomonads. It is well known that as soon as a drop of secretion has been dried all of the flagellates within it are destroyed. The advantages of treatment by drying plus antisepsis have been especially emphasized by Kleegman.²⁰

In this connection attention is drawn to the fact that 1 of 10 control patients was cured merely by repeated mechanical cleansing and drying followed by insufflation of kaolin, while in several other instances recurrences were not noted until one or two weeks after treatment.

Acetarsone has been used in trichomonas vaginitis as the active ingredient of tablets introduced under the trade name of devegan. According to Fuge,¹¹ each tablet contains 0.25 gm. of acetarsone, 0.03 gm. of boric acid, and 0.67 gm. of carbohydrate.

Although a number of the German writers have referred to devegan as a "specific," few statistics of the results of treatment are available.

Fuge¹¹ inserts 1 or 2 devegan tablets within the vagina daily for ten days. Of 100 patients treated, 60 were reported free from recurrence, while the others were still under observation. The criteria of a cure or the period through which the patients were watched for recurrences are not stated.

Hees¹⁶ claimed 95 per cent cures in over 100 cases and stated that the others responded to continued treatment.

Ackermann¹ observed 25 patients following treatment with devegan. Twelve were negative after a period of observation ranging from two to thirty-three weeks, while in 13 patients recurrences were noted.

Hajek¹⁵ and Rodecurt²³ also advocate the use of devegan.

In this country the use of devegan has been reported by Karnaky,¹⁸ who noted that 200 patients treated with this preparation were relieved of symptoms so long as they continued the use of devegan. Karnaky, however, fails to state how many of this group were permanently cured.

A mixture containing 12.5 per cent of acetarsone in equal parts of kaolin and sodium bicarbonate was recommended by Gellhorn.¹³ One teaspoonful of the mixture was insufflated by means of a powder blower designed to distribute the compound over the vaginal mucosa. The superiority of this method of introducing the arsenical lies in the fact that organisms throughout the vagina are reached, whereas the insertion of tablets leaves many parts of the vaginal mucosa untreated.

The drying effect of kaolin recommends this substance as a diluent. The value of the sodium bicarbonate is, however, questionable. The alkaline reaction of this substance tends to dissolve acetarsone. Our studies in vitro indicate, however, that solutions of acetarsone have even less trichomonadicidal activity than suspensions of acetarsone of equal percentage.

The use of borie acid and glycolized carbohydrates as employed in devegan on the basis that the acid medium and additional carbohydrate will favor the return of Döderlein's bacilli, also appears to be superfluous. It is well known that in trichomonas vaginitis the secretion is already markedly acid, Cruickshank and Sharman⁸ noting that the pH varied from 4.9 to 6.0, while Fukushima¹² found considerable concentrations of lactic acid. In cases of vaginal trichomoniasis uncomplicated by cervical infections, we have repeatedly noted the appearance of large numbers of Döderlein's bacilli, as the trichomonads disappeared after treatment by various methods. Indeed it is our opinion⁷ that the permanent reestablishment of the normal bacterial flora is the most reliable indication of a permanent cure.

Gellhorn's method of treatment has also been endorsed by J. C. Smith.²⁴ Neither of these investigators, however, have reported statistical results of their treatment.

Goldstein¹⁴ recommends the addition of 1.5 gr. of salicylic acid to Gellhorn's formula. Crossen and Crossen⁷ also believe this mixture to be efficacious.

Aldarsonc.—The synthesis of the pentavalent arsenical, aldarsonc (sodium-methylene-sulphon-amino-hydroxy-phenyl-arsonate), was re-

ently described by Raiziss, Severac and Kremens²² as preparation No. 1,717. Chemically it is a condensation product of 3-amino-4-hydroxy-phenylarsonic acid with sodium formaldehyde sulphonylate.

Aldarsone is a white amorphous powder, very soluble in water, but insoluble in alcohol, ether, acetone, or chloroform. The aqueous solution is neutral or slightly alkaline having a pH about 7.6. The product contains about 18 per cent of arsenic and 7 per cent of sulphur. In a therapeutic study of the new product in the treatment of syphilitic rabbits, Raiziss and his associates²² noted a definite spirocheticidal power which was superior to that of tryparsamide, and compared favorably with acetarsone. When given intravenously to rats and rabbits the toxicity of the drug was lower than that of acetarsone, while on oral administration to rabbits its toxicity was of the same order of magnitude as that of acetarsone.

Our studies in vitro show that aldarsone is far superior to acetarsone as a trichomonadicide.

Davis¹⁰ noted that a saturated solution of acetarsone did not kill *Trichomonas vaginalis* after fifteen minutes. In the present study, it was found that the organisms were still actively motile after being exposed to a saturated solution for one hour.

The hygroscopic quality and the lower toxicity of aldarsone were also considered to be definite advantages over acetarsone.

The free solubility of aldarsone assures its diffusion throughout the vagina, and indicates some degree of penetration. On the other hand, the insoluble acetarsone probably remains within the vagina for a longer period of time. Practically it was found that preliminary drying of the vagina plus the use of kaolin as a base insured the presence of considerable quantities of either drug within the vagina for a period of twelve to thirty-six hours.

The clinical study of aldarsone in the treatment of trichomonas vaginitis has confirmed the therapeutic efficiency which was anticipated as a result of the laboratory investigation. When administered by a thorough method of application, the clinical results were far superior to those resulting from the use of acetarsone.

Eighty-four of the 93 patients who were cured responded to an initial series of 6 treatments, 3 of which were given on consecutive days, while 3 others were given at three-day intervals. Preliminary studies have indicated that the 3 treatments which are given at daily intervals are essential for good results. We have found it to be a general principle in the treatment of trichomonas vaginitis that a number of treatments given at daily intervals are much more effective than a large series of treatments given at longer intervals.

Results of Treatment in Pregnancy.—A number of the methods described for the treatment of trichomonas vaginitis are obviously too

rigorous for application to pregnant women. As a result palliative measures, such as frequent douching, have been frequently recommended to tide the patient over until some time after delivery.

The method of treatment described in the present study, has proved to be as applicable to the obstetric as to the gynecologic patient.

Approximately three-fourths of the patients treated in the present study were pregnant women. In both the patients treated with aldarson and with acctarson, the percentage of cures was slightly higher among the pregnant women.

Recurrences.—It is apparent that the longer one continues the observation of a group of treated patients the more accurate will be the results of permanent cures. On the other hand, it is desirable to determine for any particular form of treatment that period of time after which recurrences may be considered improbable.

In general a six months' period of negativity as suggested by Davis,⁹ appears to be a reliable indication of a permanent cure for any method of treatment.

The present study indicates that a period of negativity of eight weeks after a series of 6 treatments with aldarson, administered in accordance with the technic described gives reasonable assurance of a permanent cure, when confirmed by repeated microscopic examinations.

PRINCIPLES IN TECHNIC OF TREATMENT

Although the vagina is the seat of active multiplication of the trichomonads, small numbers of organisms can frequently be recovered from surrounding structures. Bland and Rakoff⁴ have emphasized the importance of routinely treating the cervix, the urethra, the vestibule, and external genitalia, in addition to the vagina.

In the technic which we have described the entire lower genital tract is thoroughly cleansed with some mild antiseptic solution, with the purpose of mechanically removing most of the secretion and preparing the mucosa for further medication. The drying which follows the initial cleansing is an important part of the technic. In the group of patients reported this was accomplished by repeated tamponing with pledgets of soft absorbent cotton. More recently, at the suggestion of Dr. T. L. Montgomery we have used a current of warm air from a modified hair drier with much satisfaction.

We have repeatedly found occasional organisms in the secretion within the cervical canal. Although active multiplication of organisms does not appear to take place within this structure, organisms from this source may initiate a recurrence when conditions within the vagina again become suitable. On this basis tincture of metaphen

was routinely introduced into the cervical canal on cotton applicators. This preparation was found to be a good trichomonadicide and could be dried quickly.

Aekermann¹ noted trichomonads in the urethra of a number of patients who had repeated recurrences. Treatment of the urethra in addition to the vagina facilitated the cure of these patients. In a number of the present group of patients plugs of secretion containing trichomonads were recovered from the urinary meatus. An aqueous solution of metaphen 1:500 was therefore routinely instilled in the urethra and also carried into the paraurethral recesses.

SUMMARY

1. Laboratory and clinical investigations were conducted to determine the efficacy of a new soluble pentavalent arsenical, aldarson (sodium-methylene-sulphon-amino-hydroxy-phenyl-arsonate) in the treatment of trichomonas vaginitis. The results were compared with those obtained with acetarson.

2. Studies in vitro indicated that aldarson has a definite trichomonadidal power, which is many times that of acetarson. The trichomonadidal power of aldarson was not inhibited by human blood serum.

3. One hundred women with trichomonas vaginitis were treated by the insufflation of 0.5 gm. of aldarson, diluted with kaolin, following preliminary cleansing of the vagina and vulva with a diluted tincture of green soap and water, instillation of tincture of metaphen into the cervix, and an aqueous solution of metaphen 1:500 into the urethra. A total of 91 women remained free from trichomonas during a period of three to nine months following treatment. Of these 84 women who remained negative after a series of 6 treatments, 5 required an additional series of 6 treatments, and 2 were cured after 2 additional series of treatments.

4. Of 25 women treated by a similar technic with acetarson, only 12 or 44.4 per cent remained free from trichomonas, while 13 had repeated recurrences.

5. It is concluded that clinical experience as well as laboratory studies indicate that aldarson is much superior to acetarson in the treatment of trichomonas vaginitis.

6. Approximately three-fourths of the women treated were gravid. The results of treatment among the pregnant group with both acetarson and aldarson were slightly better than among the nongravid group.

7. Among a total of 36 recurrences which were noted following treatment with aldarson 22 were detected during the first two weeks following treatment, while none were noted either clinically or by microscopic study after eight weeks.

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1621 SPRUCE STREET.

MANAGEMENT OF SECONDARY AMENORRHEA OF FUNCTIONAL ORIGIN

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SECONDARY amenorrhea of functional origin remains a perplexing therapeutic problem. Attempts to reestablish the menses by the use of gonadotropic and estrogenic substances alone have not proved to be a panacea for this disorder. Better results have been obtained by the use of thyroid extract and by x-ray "stimulation" of the ovaries and pituitary gland. Pelvic massage, dilatation of the cervix, dietetic regimes, and oral preparations of various internal secretory glands have also appeared to be effective in "curing" amenorrhea.

One conclusion which may be drawn from the use of such varied therapeutic measures is that the mechanism of menstruation, while essentially controlled by the anterior pituitary gland and the ovaries, is not absolutely independent of other influences, which may be endocrine, physical, or even psychic in origin. This being true, better results should be obtained if the specific physiologic disturbance in any individual case could be ascertained in advance of treatment, and then to apply the therapeutic agent found most suitable for the particular disorder. It is unreasonable to expect estrogenic hormone to be as effective in amenorrhea due to hypothyroidism as it is in underfunction of the

ovaries. Likewise it is superfluous to use gonadotropic hormone in instances of ovarian failure since this substance is already present in excess in these cases.

To prevent misapplication of useful therapeutic agents, R. T. Frank et al.¹ advocated a specific routine procedure in the study of functional amenorrhea as a basis for the rational interpretation of its etiology and cure. The report which follows is predicated on a similar routine, with results warranting a more detailed analysis.

Since 1933, twenty-five cases of functional amenorrhea were observed at the Gynecological Endocrine Clinic of Lebanon Hospital. With few exceptions, these women had received one or more unsuccessful courses of treatment prior to registration at the clinic, including the use of pills, hypodermic medication of ovarian and pituitary sex hormones, and x-ray "stimulation" of the pituitary gland and the ovaries. As a whole, these patients typified the more severe forms of secondary amenorrhea. Their ages ranged from seventeen to thirty-six years, the average age being twenty-five years. All of the women in this series had menstruated prior to the onset of amenorrhea. Eighteen patients complained of absent menstruation for periods of six months to three years. Seven patients were amenorrheic for less than six, but more than three months. Each case was carefully studied to exclude non-functional causes of amenorrhea, arising from pathologic states of the genital organs, from nutritional disorders, or from tuberculosis. A basal metabolism and an analysis of the urine for gonadotropic and estrogenic hormones were then performed. The clinical and laboratory data when completed were analyzed for etiologic leads upon which to base the treatment. The method of therapy was adapted to each case. Menstruation was restored, and the regularity of the menstrual cycles greatly improved in 60 per cent of the patients.

Patients with diminished uterine bleeding but regular cycles, and those whose menstrual intervals never exceeded two months, were not included in this study as these women become easily adjusted to their irregularity and seek professional advice only when concerned about the presence of a pregnancy.

The question of most importance in any case of amenorrhea is whether the ovaries are functioning. This may be determined in three ways: by the history, by biopsy of the endometrium, and by hormonal analyses.

A history of cyclically recurrent low abdominal pains and breast pains similar to those which the patient had previously experienced with menstruation suggests the presence of some ovarian activity.¹ This was present in eight patients, all of whom proved to have ovarian function on hormonal analyses (Table I). The demonstration of a "premenstrual" or "secretory" type of endometrium by curettement not only indicates ovarian function but also demonstrates a proper

balance in the elaboration of follicular and lutein hormones. Biopsy of the endometrium by means of the suction curette-cannula* I have devised can be performed in the office with very little discomfort to the patient. Finally, ovarian activity may be detected by analyses of the blood or the urine for estrogenic and gonadotropic substances. On the basis of the analyses, it is possible to determine not only the presence of ovarian activity but also whether the follicular function of the ovaries is normal or diminished.

Another essential factor to be determined in a case of secondary amenorrhea is whether ovarian function has ceased completely. If the

TABLE I. SYMPTOMATOLOGY OF AMENORRHEIC PATIENTS

CASE	AGE	PELVIC PAIN	BREAST PAIN	FLUSHES	DURATION OF AMENORRHEA
<i>Group 1—With Normal Follicular Function</i>					
1	21	Absent	Absent	Absent	10 months
2	23	Absent	Absent	Absent	3½ months
7	22	Absent	Absent	Absent	3 months
8	24	Present	Present	Absent	10 months
9	29	Present	Absent	Absent	3 months
11	23	Present	Present	Absent	3 months
15	31	Absent	Absent	Present	3 months
19	28	Absent	Absent	Absent	12 months
<i>Group 2—With Diminished Follicular Function</i>					
4	27	Absent	Present	Absent	3 years
5	28	Present	Absent	Present	6 months
12	17	Absent	Absent	Absent	11 months
13	25	Absent	Absent	Absent	5 months
14	29	Absent	Absent	Absent	3 years
17	18	Absent	Absent	Absent	5 months
18	19	Present	Absent	Absent	6 months
20	19	Absent	Absent	Absent	10 months
21	18	Absent	Absent	Absent	4½ months
23	25	Present	Absent	Present	8 months
24	36	Absent	Absent	Present	1 year
25	30	Absent	Present	Absent	2 years
<i>Group 3—With Ovarian Failure</i>					
3	34	Absent	Absent	Present	6 months
6	31	Absent	Absent	Present	8 months
10	32	Absent	Absent	Present	10 months
16	29	Absent	Absent	Present	13 months
22	17	Absent	Absent	Absent	9 months

menopausal state exists, obviously therapeutic efforts are bound to fail even though uterine bleeding may be restored by substitution therapy. Here again the history, type of endometrium, and hormonal analyses give valuable information.

A history of "hot flushes" and prolonged amenorrhea is generally interpreted as a menopausal manifestation. Eight patients had these symptoms (Table I). Four were found to exhibit some follicular activity and two of them, Cases 5 and 15, both young women, subsequently reestablished their menstrual cycles. The other four patients

*Manufactured by the American Cystoscope Makers, Inc., New York City.

were proved, by hormonal analyses, to have an early климаeterium. Therefore, unless the "flushes" are associated with definite hormonal changes indicating complete cessation of ovarian function, no significance can be attached to its presence.

The finding of marked genital atrophy, in the form of ill-defined labia, conical and narrow vagina, and small uterus, also gives no index of the ovarian function. Advanced cases of genital atrophy were found among women with normal follicular activity as well as those with diminished or absent gonadal function. Menstruation was restored or improved in four of the twelve patients with genital atrophy. One patient, Case 25, later became pregnant, thus indicating the extent to which the reproductive mechanism may recover.

The demonstration of a "resting" endometrium by curettement does not preclude ovarian activity even if obtained on two or more successive weekly examinations. At most it signifies an inadequate production of estrogenic hormone.

TABLE II. ESTROGENIC FUNCTION OF OVARIES AS DETERMINED BY HORMONE ANALYSIS OF THE URINE

Group 1	Estrian present in normal or excessive amounts Prolan-A absent or occasionally present	Normal follicular function
Group 2	Estrian present in small amounts Prolan-A absent or occasionally present	Diminished follicular function
Group 3	Estrian absent Prolan-A absent or occasionally present	Diminished follicular function
Group 4	Estrian absent Prolan-A persistently present	Ovarian failure

The best method of ascertaining complete failure of ovarian function is by means of hormonal analyses of the blood and/or the urine. At menopause an excess of prolane A, the gonadotropic hormone elaborated by the anterior pituitary gland, can be demonstrated in the circulating blood.² It is also present after complete extirpation of both ovaries or after radiation castration. Other investigators have shown that prolane is consistently present in the urine under similar circumstances.

From the foregoing, it is clear that hormonal analyses gives the most reliable index of the status of the estrogenic function of the ovaries. Therefore it should be an essential step in the study of amenorrhea. This was performed in every case in this study, and repeated at various intervals after treatment to detect any changes. Unfortunately the relation of progesterin to amenorrhea was not studied because the method of identifying this lutein hormone, that of Allen,³ is too expensive and time-consuming for a routine laboratory procedure.

The method of hormonal analysis adopted was that advocated by Kurzrok and Ratner.⁴ Each patient brought a full twenty-four-hour collection of urine once weekly for four consecutive weeks. The specimens were measured and divided into two portions, one of which was

tested for prolan and the other for estrin. The details of the extraction and hormonal identification followed by the author are adequately described in a previous communication.⁵

The hormonal reactions obtained are grouped in Table II, and are similar to those described earlier by Kurzrok.⁶ Similar groupings have also been described by Frank⁷ both in the blood and in the urine.

TABLE III. ENDOCRINE TYPES WITH SECONDARY AMENORRHEA

1. Hypothyroidism	<a—with obesity
2. Hypopituitary obesity	<b—with low basal metabolism
3. Hypoovarian obesity	
4. Eunuchoidism	
5. Eumorphic females	<a—with normal follicular function
	<b—with diminished follicular function
	<c—with ovarian failure

According to Smith and Smith,⁸ the method used in this study extracts only about 60 per cent of the total amount of estrin present. Therefore the failure to demonstrate estrogenic hormone does not absolutely exclude its presence in small amounts. For that reason, Groups 2 and 3 should be considered as a single group with Group 3 representing the severer grade of dysfunction.

Having established the state of ovarian activity, it is equally essential to seek for evidences of other glandular disturbances. The prepituitary lobe and the ovaries, though the principal regulators of the menstrual cycle, are in turn influenced by other organs of the endocrine system, particularly the thyroid, the adrenals, and even the pineal gland. Furthermore, it is known that psychogenic and neurogenic disturbances may alter menstrual activity. Therefore it is necessary to determine the basal metabolism, and to note any alterations in weight, hirsutism, character of the skin, anthropometric variations, enlargement of the thyroid, and size of the breasts, all of which are directly or indirectly controlled through the activity of the endocrine system. The physical variations may be sufficiently pronounced to permit of a fairly accurate diagnosis of the gland at fault. Thus we have learned to distinguish clinically the hyperthyroid, the hypothyroid, the Frölich syndrome, and so forth. This differentiation, however, is not always possible and not often recognized unless carefully noted.

On the basis of the physical examination and the laboratory criteria, the patients in this study could be appropriately reclassified into the endocrine types shown in Table III. This classification served as a working basis for therapy and proved to be most helpful from a prognostic standpoint. A more detailed description of the cases is tabulated in Tables IV and V.

Patients Evidencing Hypothyroidism with Obesity (3 cases).—

These three patients not only exhibited the rather typical shoulder deposition of fat, but also thickening of the dermis, dryness and loss of hair, and lassitude.

TABLE IV. SECONDARY AMENORRHEA

CASE	AGE	DURATION AMENORRHEA	OVER-WEIGHT	BASAL METAB.	GENITAL ATROPHY	SIZE OF BREASTS	HORMONE		THERAPY	RESULTS
1a—Cases With Hypothyroid Obesity										
1	21	10 months M = 12 x 4 - 6 mo. x 7	+39	?	Moderate	Normal	++	0	Diet + thyroid	Bled 2 wk. later. Then reg. every month for 2½ years
8	24	10 months M = 14 x 30 d x 4 → D + C	+37	+ 7	Moderate	Normal	++	0	Diet	Lost 15 pounds → menses ensued → pregnant → quite reg. since
20	19	10 months M = 16 x 3 - 9 mo. x 4	+38	-10	Marked	Normal	+	0	Thyroid	Bled every 1½ to 2 mo. during the next 2 years
1b—Cases With Low Basal Metabolism										
7	22	3 months M = 14 x 3 - 6 mo. x 4	-3	-27	None	Normal	++	0	Thyroid	Bled every 1-3 months during next 3 years
13	25	5 months M = 14 x 2 - 3 mo. x 5	-4	-13	None	Atrophic	+	0	Thyroid	Bled every 1-2 months during next 8 months
23	25	8 months M = 12 x 28 d x 2	+8	-15	None	Normal	0	0	“Stim” x-ray of ovaries	No improvement
10	32	10 months M = 14 x 24 d x 4	0	-20	Marked	Atrophic	0	+	“S” x-ray ov. “D” x-ray pituit.	No improvement
2—Cases With Hypopituitary Obesity										
2	23	3½ months M = 12 x 1½ - 3 mo. x 5	+44	-6	Marked	Pendulous	++	0	Thyroid	No improvement
24	36	1 year M = 13 x 1 - 3 mo. to 1922 then amen. 6 yr.,	+34	-1	Marked	Pendulous	0	0	Follutein + amniotin	No return of menstruation. Menstrual symptoms +
6	31	8 months 1 yr. M = 13 x 28 d x 3	+66	?	Marked	Pendulous	0	+	Thyroid	No improvement
3—Cases With Hypoovarian Obesity										
11	23	3 months M = 13 x 28 d x 5 to 1921 then every 3 - 12 mo.	+23	-7	Marked	Normal	++	0	Follutein + amniotin	Bled every 1-2 months during next 3 years
21	18	4½ months M = 14 x 3 - 9 mo. x 4	+24	-7	None	Normal	+	0	“Stim” x-ray of ovaries	Bled every month during next 2½ years
4—Eunuchoidism										
12	17	11 months M = 15 x 1 - 2 mo. x 5	-8	-4	Marked	Normal	0	0	Foll. + amniot. thyroid “S” x-ray ov.	No improvement

TABLE V. EUMORPHIC FEMALES

CASE	AGE	DURATION AMENORRHEA	OVER- WEIGHT	GENITAL ATROPHY	SIZE OF BREASTS	THERAPY	RESULTS
<i>a—Normal Ovarian Estrogenic Function</i>							
9	29	3 months M = 14 × 2 - 10 mo. × 4	+18	None	Normal	None	Bled every 1-1½ mo. following examination
15	31	3 months M = 13 × 30 - 45 d × 8	0	None	Normal	None	Bled every 30-35 days following examination
19	28	12 months M = 15 × 28 d × 4 → 26 yr. then every 1-3 mo.	+14	Marked	Atrophic	Refused	No improvement
<i>b—Diminished Ovarian Estrogenic Function</i>							
4	27	6 months M = 11 × 28 d × 4	- 6	None	Normal	"Stim," x-ray of ovaries	No improvement
5	28	6 months M = 12 × 28 d × 8	- 2	Moderate	Normal	Dilatation of cervix	Bled every 28 days following treatment
14	29	3 years M = 13 × 28 d × 4 → 21 yr. then every 1½-3 mo.	+ 8	Marked	Normal	Follutein + amniotin	No return of menstruation. Menstrual symptoms +
17	18	5 months M = 16 × 3 mo. × 5	0	Marked	Normal	Follutein + amniotin	Bled every 1 to 1½ months during next 3 years
18	19	6 months M = 12 × 1-3 mo. × 5, then menorrhagia 1½ yr. 2 years	-14	None	Normal	"Stim," x-ray of ovaries	Bled regularly q 28 d. for 5 mo. → menorrhagia
25	30	Only menses 2 yr. ago	- 5	Marked	Normal	"Stim," x-ray of ovaries	Bled once. Normal pregnancy followed. Menses regular
<i>c—Ovarian Failure</i>							
3	34	6 months M = 11 × 28 d × 4	0	None	Atrophic	Refused	No improvement
16	29	13 months M = 13 × 28 d × 5	- 4	Marked	Atrophic	"Dep," x-ray of pituitary	No improvement
22	17	9 months M = 13 × 4-6 wk. × 4	+ 3	Marked	Atrophic	"Stim," x-ray of ovaries	Menses recurred—became regular after 8 months

Despite the prolonged period of amenorrhea (ten months), ovarian function was normal in two women and diminished in one. This was interpreted as indicating a hopeful prognosis. The patients were placed on a reducing diet and desiccated thyroid extract (Armour).

The patient in Case 1 began to menstruate regularly after taking thyroid for only two weeks, perhaps too soon to attribute the clinical cure to the use of the drug. Incidentally this woman, two years previously, established menstrual regularity for several months, after a twelve-month period of amenorrhea, merely by losing 40 pounds in weight. The amenorrhea recurred with the return of her adiposity. Frank has emphasized this relationship between obesity and amenorrhea before.¹

The patient in Case 8 began to menstruate after a loss of 15 pounds and became pregnant six months later. A reduction in weight accomplished by dieting alone (thyroid tolerance poor) apparently aided in her cure.

Case 20 failed to lose weight but menstruated more frequently as long as she remained on thyroid medication.

Patients Evidencing Hypothyroidism without Obesity (4 cases).—These patients presented no evidence of diminished thyroid activity other than a low basal metabolism. The rates varied from -13 to -27. Mussey and Haines¹⁰ reported 27 similar cases of amenorrhea associated with low basal metabolism, none of whom presented any organic disease to which to attribute the lack of bleeding.

Patients in Cases 7 and 13 received thyroid medication and shortly thereafter showed distinct clinical improvement.

The patient in Case 23 was a severe diabetic. Thyroid extract was withheld lest it might influence the glucose tolerance and thus interfere with the administration of insulin. She was reluctant to try any hypodermic medication, so that x-ray "stimulation" of the ovaries* was resorted to. Menstruation, however, failed to ensue. Further hormonal analyses likewise revealed no improvement.

Case 10 was the only patient with hypothyroidism whose ovarian function, as determined by hormonal analyses, had ceased completely. Thyroid therapy proved unsuccessful. This is not surprising in view of the poor prognosis indicated by the hormonal findings.

Of the seven patients with hypothyroidism, five were clinically improved. The prognosis in this type of patient is much better than in any of the other endocrine types. It is with good reason therefore, that Novak was led to conclude that "thyroid extract still remains as the sheet anchor in the treatment of functional amenorrhea."¹¹

Patients with Hypopituitary Obesity (3 cases).—These patients had pendulous breasts, large abdominal aprons of fat, and were from 34 to 66 pounds overweight. They also presented an acromegalic facies.

The patient in Case 2 was found to have normal follicular function of the ovaries. Basal metabolism was -6. Her tolerance for thyroid extract, even in small doses, was poor. Despite all dietary control she continued to gain weight. The menstrual intervals, which formerly lasted three months, now lengthened to six months.

The patient, Case 24, before coming under my observation, had been treated with extracts of the thyroid gland and ovaries, and also by irradiation of the pituitary gland and the ovaries without any beneficial results. Hormonal analyses of the urine revealed no estrin or prolan (Group 3 reaction, Table 2). Accordingly, these substances were given three times weekly for several weeks in the form of amniotin† and follutein.† However, menstruation did not ensue. It is interesting

*The technic of x-ray therapy was performed under the direction of Dr. C. L. Okrainetz of the Radiotherapy Department, Montefiore Hospital, New York City.

†These preparations were generously donated by E. R. Squibbs and Sons through Dr. J. J. Durrett. The amniotin assayed at 50 R.U. per c.c. and the follutein at 100 R.U. per c.c.

to note that following the injections, the patient experienced low abdominal pains and tingling of the breasts, symptoms which did not exist prior to treatment. After treatment was discontinued, these symptoms failed to recur. This clinical response to hormonal therapy probably represents a gonadal reaction, and as such, is a helpful prognostic sign. The failure to initiate uterine bleeding in this patient may have been due to insufficient dosage of the hormones.

The third patient, Case 6, showed complete ovarian failure on hormonal analyses. She failed to respond to treatment, which was expected.

Patients with Hypoovarian Obesity (2 cases).—The obesity in these two patients was somewhat generalized but predominated about the thighs and hips. There were no changes in the hair or skin. The breasts were normal.

Although the follicular hormonal excretion of Case 11 reached normal values, most of the specimens examined gave subnormal amounts. For that reason, the patient was placed on amniotin (450 R.U.) and follutein (300 R.U.) weekly for three months. Subsequently the menstrual cycles recurred every one to two months instead of from three- to twelve-month intervals. The improvement in menstruation was accompanied by a marked improvement in the function of the ovaries, demonstrated by further hormonal analyses.

The other patient in this group, Case 21, was treated similarly but the treatment had to be discontinued because of allergic manifestations following the injections of amniotin. She was also intolerant of small doses of thyroid extract. As a last resort, a "stimulating" dose of x-ray was given to both ovaries. Menstruation set in four weeks later, and since then has recurred every one to one and one-half months instead of the former three to nine-month intervals. Hormonal analyses showed corresponding improvement in ovarian function.

Eunuchoidism (1 case).—Berkow¹² described several cases of eunuchoidism with amenorrhea. These patients were of normal mental and physical development, except for a hypoplasia of the genital tract and a disproportion of bony growth, the extremities being relatively too long for the trunk. The growth disturbance is due to a lack of ovarian influence on the ossification centers of the long bones during early adult life. The hypofunction of the ovaries is in turn due to a deficiency of the gonadotropic function of the anterior pituitary lobe.

Case 12 was of this type. Hormonal analyses revealed no excretion of follicular hormone. Treatment with amniotin, follutein, thyroid extract, and "stimulating" doses of x-ray to the ovaries were of no avail. On one occasion, after receiving a total of 2,000 R.U. of amniotin in oil in ten days, the patient excreted follicular hormone for the first time. This was found to be exogenous hormone, because when treatment was discontinued no further estrin could be demonstrated. This patient has been observed for three years. The amenorrhea has persisted. Otherwise she has continued to enjoy excellent health.

According to Frank,¹³ the prognosis in this type of female is poor but by no means hopeless, as clinical improvement may occasionally occur.

Eumorphic Females with Normal Basal Metabolism (12 cases).—These patients represented the normal type of female, being of average weight, with normal basal metabolic rates, and exhibited no stigmas of endocrine dysfunction other than the menstrual disturbance. Although clinically they constituted one complete group, hormonal analyses indicated a pronounced difference in their estrogenic function. To facilitate discussion, they are subdivided as follows:

- A. Cases exhibiting normal follicular function
- B. Cases exhibiting diminished follicular function
- C. Cases exhibiting complete ovarian failure

Cases Exhibiting Normal Follicular Function (3 cases).—Two patients, Cases 9 and 15, menstruated spontaneously following their first visit to the clinic and

continued their cycles with greater regularity thereafter. The explanation for this is not clear in either instance. Anspach and Hoffman¹⁴ reported spontaneous cures of some cases of amenorrhea by pelvic massage. They attribute the beneficial results to a disruption of atretic follicles, retention cysts, and persistent corpora lutea which are impediments to egg-ripening and ovulation.

The third patient, Case 19, had previously been treated unsuccessfully with various pills as well as radiation of the pituitary gland and the ovaries. Analyses of the urine revealed normal quantities of follicular hormone. Unfortunately, she was too discouraged by former failures to cooperate intelligently. Consequently no treatment was given at the clinic. She was last seen in July, 1935, with an amenorrhea of three years' duration. Hormonal analyses showed the ovaries to be still functioning, but at a lower level.

*Cases Exhibiting Diminished Follicular Function (6 cases).—*Menstrual function was improved in four of the six patients in this group.

The patient in Case 5 menstruated for two days following a biopsy of the endometrium. This was neither traumatic bleeding nor blood from a hematometra, because there was a slight delay in its appearance after the biopsy, and because the bloody fluid was typically menstrual in character. Subsequently she continued to menstruate regularly. It is interesting to note that the biopsy material failed to show a "premenstrual" mucosa. Possibly the uterine bleeding in this case is of the "anovulatory" type described by Novak.¹⁵ Further studies on this subject are being made.

The patient in Case 17 had previously received thyroid extract without any beneficial effect. Treatment with estrogenic and gonadotropic hormones was instituted, a total of 1700 R.U. of amniotin and 1500 R.U. of follutein being given in three months. Following this, the menstrual intervals diminished from three-month intervals to cycles of one and one-half months. Hormonal analyses revealed a distinct improvement of the estrogenic function months after treatment had been discontinued.

Case 18, a single girl of nineteen years, originally came under observation because of menometrorrhagia. The bleeding stopped spontaneously and then became amenorrheic for six months. At first a pregnancy was suspected and apparently confirmed by the presence of a softened uterus and a positive Friedman pregnancy test. However, the uterus failed to enlarge and a second pregnancy test was negative. On this basis a diagnosis of a persistent lutein cyst was made, and x-ray "stimulation" of the ovaries was given. Shortly after this therapy, menstruation recurred and remained regular for several months. Lately the menorrhagia has returned, probably because of further cystic change in the ovaries.

The patient in Case 25 also received x-ray "stimulation" of the ovaries and immediately afterward menstruated. This was the first menstrual flow in two years. Hormonal analyses revealed a greatly improved ovarian function. When the next period failed to materialize, she was found to be pregnant and eventually was delivered of a normal full-term infant. Menstruation then recurred regularly for several months, only to be again interrupted by another amenorrheic interval due to a second pregnancy.

X-ray "stimulation" to the ovaries was tried unsuccessfully on patient in Case 4. Glandular therapy was advised prior to this but refused by the patient.

Patient in Case 14 was given 5,200 R.U. of amniotin and 10,000 R.U. of follutein over a period of five months with no menstrual response. Hormonal analyses, performed during intervals when she was free of treatment, revealed 3.5 to 6.6 R.U. of estrin (normal amount varies from 10 to 20 R.U.) where previously none could be demonstrated. This, in itself, indicated a distinct improvement in ovarian function. It is possible that, had larger doses of amniotin been given, such as are now available, a better result might have been obtained.

Cases Exhibiting Complete Ovarian Failure (3 cases).—This group was interpreted as typifying early menopause because of the similarity of the hormone findings to those present during natural or artificially induced menopause.

Two of the patients, aged twenty-nine and thirty-four years, respectively, were already experiencing "menopausal flushes." The older woman, Case 3, was content to know that menstruation would not recur and refused any treatment. The other patient, Case 16, received "depressive" doses of x-ray to the pituitary region with the hope that prolactin production would be diminished. However, no clinical or hormonal changes were noted. Her "flushes," amenorrhea, and hormonal findings continued unabated.

The remaining patient in this group, Case 22, was a young girl of seventeen, who became amenorrheic immediately following an appendicectomy. Whether the operation was an etiologic factor in producing the menstrual dysfunction is difficult to say. It is also hard to believe that the ovaries of so young a girl should have exhausted all primordial follicles unless we assume that there existed a congenital deficiency of such structures. It was more rational to assume that some inhibitory force was present which prevented the proper cyclical development of the primordial follicles. Such a factor might well be a persistent lutein cyst, as this body is known to inhibit maturation of the follicles. The excess of prolactin was interpreted as an attempt on the part of the anterior pituitary gland to reactivate the ovaries.

From a therapeutic standpoint, it is obviously wrong to give this patient additional gonadotropic substance. Patients with complete ovarian failure have much larger quantities of this hormone circulating in their blood than may be administered hypodermically. Follicular hormone in large amounts may induce an artificial flow but it is mere substitution therapy. The uterine bleeding resulting therefrom will cease after discontinuing therapy. No stimulating effect on the ovaries will take place.¹⁶

The only remaining agent which might prove of value to such a case is the x-ray. So-called "stimulating" doses were given to the ovaries and menstruation followed two weeks later. Hormonal analyses of the urine then revealed the presence of subnormal amounts of estrin but no diminution in the content of prolactin A. After two menstrual periods, the amenorrhea recurred. Another course of x-ray "stimulation" was given. The patient then began to experience the menses at monthly intervals, but actual bleeding did not take place until eight months later. Since then, she has menstruated regularly each month, and recent hormonal analyses revealed normal quantities of follicular hormone. However, prolactin A excretion was still present in every specimen. This prognosticates a probable recurrence of the amenorrhea.

DISCUSSION

The pituitary-ovarian control of menstruation has been generally accepted, though much remains to be clarified. This control is affected in many endocrinopathic disorders and accounts for the frequent association of obesity with amenorrhea.¹ The keen observer will recognize differences in the fat deposition, depending upon the gland or glands at fault." Alterations in bony growth, and in the character of the skin and skin appendages will frequently be noted in any large series of long-standing secondary amenorrheic patients. A low basal metabolism is commonly present.

Unfortunately the physical examination alone gives no inkling of the ovarian function. Two individuals, seemingly alike physically, may differ considerably in regard to their gonadal activity. Many failures

in therapy are attributable to this difference. It is most advisable, in patients with prolonged amenorrhea, to perform an analysis of the blood and/or the urine for estrogenic and gonadotropic hormones. This information readily reveals the degree of ovarian follicular activity or inactivity. It yields tangible evidence upon which to base a prognosis. Hormonal analysis is unnecessary where the amenorrheic intervals are of short duration.

From a therapeutic standpoint, desiccated thyroid extract and x-ray "stimulation" of the ovaries proved to be the best agents in restoring menstruation in this series of cases. They accounted for two-thirds of the cures.

The part played by the thyroid gland in inducing menstruation is not fully understood. The stimulating effect on the ovaries may be brought about indirectly through stimulation of the anterior pituitary lobe, and directly by the power of thyroxine to increase cellular activity generally. When the ovarian function is normal in the presence of a coexisting hypothyroidism, as in Cases 1 and 7, the manner of action of thyroid extract is not quite clear. Possibly the bleeding results from some alteration in the endometrium. This is merely a suggestion. As a matter of fact, despite all the theories pertaining to the mechanism of menstruation, the actual cause of the menstrual flow, the so-called "bleeding factor," is as yet unknown. Until this is more clearly understood, the basis for thyroid therapy must rest on theoretical considerations only.

Thyroid extract is not always well tolerated, even in small doses. The patients must be frequently re-examined for signs of thyroid intoxication, and the basal metabolism rechecked. The amount used was the largest dose tolerated by the patient without producing toxic symptoms. As a rule, it ranged between 3 and 6 gr. of thyroid extract (Armour) daily.

It is erroneous to speak of x-ray irradiation as a "stimulating" agent. It is always a destructive force. When "stimulating" effects follow its use, it is due to the destruction of some inhibitory force. This was shown experimentally by Van Pée and Simon.¹⁷ They irradiated the ovaries of mature rabbits and dogs, and demonstrated a selective sensitivity of the various structures in the ovaries to the rays. The most sensitive was found to be the maturing follicle, and the least sensitive to be the corpus luteum, due in all likelihood to the less mature and more actively growing granulosa cells of the follicle.

Whether this effect of x-ray on animal ovaries is equally true of human ovaries is not known, although clinical observations indicate it to be so. Cystic ovaries have long been known to cause delay in menstruation. The removal of these cysts by partial oophorectomy or by puncture has been followed by the re-establishment of menstruation.

The destruction of similar cystic structures by the x-ray might explain the "stimulating" effect of irradiation obtained in Cases 18 and 22.

Rongy,¹⁸ in 1927, was the first in this country to describe the beneficial influence of x-ray "stimulation" in secondary amenorrhea. Since then several reports have appeared substantiating these results, the latest being that of Mazer and Spitz.¹⁹ These authors stress the fact that x-ray should be a measure of last resort because of the possibility of inducing castration atrophy despite the control of dosage.

The hope that the newer ovarian and prepituitary sex hormones would prove as effective for amenorrhea as insulin is for diabetes mellitus, or thyroxine for hypothyroidism, has not been fulfilled. This is due to the fact that, in most instances, the amenorrhea exists as a symptom and not as a disease entity. It is often part of a pluriglandular syndrome involving more than one specific hormone.

Estrogenic and gonadotropic hormones should be used primarily in cases exhibiting diminished ovarian function. Patients with ovarian failure (menopause-like states) are not proper subjects for glandular therapy and attempts to cure them with the sex hormones are misapplications of useful therapeutic agents.

Amniotin and follutein were given to six patients, all of whom were demonstrated to have poor ovarian follicular activity. Menstruation was re-established with greater regularity in two (Cases 11 and 17). One woman, Case 14, exhibited an improved follicular function of the ovaries but failed to menstruate. Another, Case 24, experienced the menses while under treatment, but the hormonal findings and the amenorrhea continued unchanged. Case 21 was allergic to amniotin, a contraindication for continuing this treatment. The sixth patient, Case 12, failed to respond in any manner to hormonal therapy.

Since this study was begun, the strength of amniotin has been increased to 400 R.U./c.e. and to 2,000 R.U./c.e., an improvement that more nearly approximates the amount necessary to build a proliferative endometrium in the human uterus. Kaufmann²⁰ showed that 25,000 to 50,000 R.U. of estrogenic hormone per month, reinforced by 25 to 50 rabbit units of progestin (corpus luteum hormone) were required to induce true menstruation in human castrates or postmenopausal women. With functioning ovaries, less of the follicular and lutein hormones is needed, but the dosage for any individual case can be determined only by trial and error.

The future for hormone therapy was best expressed by R. T. Frank²¹ who stated that "the prospect that eventually hormone therapy of gynecologic and obstetric functional disturbances will be put on a rational and effective basis is excellent. Such result will develop from well-selected, carefully controlled and objectively studied series of cases; perhaps by trial and error, certainly not by machine gun type of endocrine drugging to which the profession is becoming addicted."

CONCLUSIONS

1. A series of 25 cases of secondary amenorrhea of functional origin are reported. Most of these cases had failed to respond to the usual therapeutic measures before presenting themselves for study. Menstruation was restored and the regularity of the menstrual cycles greatly improved in 60 per cent of these patients.

2. The patients were classified according to their endocrine type and to the status of their ovarian function. This was determined by noting physical stigmas of endocrine dysfunction, by the basal metabolic rate, and by hormonal analyses of the urine for estrogenic and gonadotropic hormones.

3. The prognosis for restoration of menstruation was best in those women with normal ovarian function, and poorest in those with ovarian failure.

4. The treatment regime, in any individual case, depended upon the group to which the patient conformed.

5. The procedures effective in the highest percentage of cases were desiccated thyroid extract (Armour) and x-ray "stimulation" of the ovaries. Next in effectiveness were amniotin (Squibbs) and follutein (Squibbs).

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A few cases are reported of persistent headache associated with the nursing period, which characteristically disappeared on weaning. No underlying cause was discoverable in any of the cases. The condition is rare and is most likely to occur in multiparas. It is usually seen in those of very poor economic circumstances and poorer physical condition, where nursing is an added burden. Dental caries is often an associated but not a causative factor. Rigid prenatal care and improvement of the general condition during the puerperium are essential in treatment. Weaning is the final therapeutic measure, if the symptoms justify it.

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THE CELL VOLUME FOLLOWING DELIVERY AND ITS RELATION TO BLOOD LOSS AND POSTPARTUM INFECTION*

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IN A RECENT study of the third stage of labor by the author, it was demonstrated that the incidence of puerperal infection was proportional to the blood loss. The reduction of infection, therefore, involves not only the elimination of the factors during pregnancy, labor, and delivery, which influence the blood loss, but also the proper treatment of the patient who has sustained a hemorrhage.

There are two factors which are definitely established at the present time. First, the blood loss increases with the weight of the patient, and second, the seriousness of the hemorrhage is inversely proportional to the body weight, for example, a patient weighing 90 kg. will tolerate a loss of 1,000 c.c. much better than the patient weighing only 50 kg. Since we also know that the blood volume is proportional to the body weight, we have expressed the blood loss as a percentage of the weight of the patient. Thus:

$$\frac{\text{Blood Loss (c.c.)} \times 100}{\text{Wt. of Pat. (Kg.)} \times 1000} = \frac{\text{Blood Loss (c.c.)}}{\text{Wt. (Kg.)} \times 10} = \text{Per cent Blood Loss.}$$

For example, if the blood loss was 260 c.c. and the weight of the patient 65 kg., the percentage of blood loss would be $\frac{260 \text{ c.c.}}{65 \text{ kg.} \times 10} = 0.4$ per cent. Most of our

patients are weighed before and after delivery, and the weight before delivery was used in this calculation. Where this was not obtained the last weight in the prenatal course was used. By this method, a blood loss of 600 c.c. would be 1.0 per cent in the average patient weighing 60 kg. and would therefore be considered a hemorrhage, whereas it would be only a 0.66 per cent loss for a patient weighing 90 kg. On this basis, the percentage of loss is much more valuable than the actual loss in cubic centimeters.

Determining the incidence of postpartum infection on this basis, we have the graph as represented in Fig. 1. This includes all patients who had a rise in temperature to 38° C. or more during two twenty-four-hour periods and excluding the first twenty-four hours after delivery. The graph represents the incidence of infection in 1,431 cases of premature and full-term vaginal deliveries which were discharged from the hospital between May 1, 1935, and Feb. 1, 1936. The blood loss was measured by the method described in an earlier publication.⁷

*Presented before the Section of Obstetrics and Gynecology, Buffalo Academy of Medicine, April 15, 1936.

Ninety-two per cent of all the patients with vaginal deliveries during this period are included in Fig. 1. In the other 8 per cent of the cases, including deliveries on the isolation floor which is not equipped with a measuring apparatus, the blood loss was not measured for various reasons.

For blood losses less than 0.3 per cent, the incidence of infection remains fairly constant around 6.5 per cent. Above this value it rises rapidly until the blood loss reaches 0.7 per cent. This initial rise increases the incidence of infection by over 100 per cent. For losses between 0.7 per cent and 1.0 per cent the incidence of infection is again constant. A secondary rise begins at the hemorrhage range,

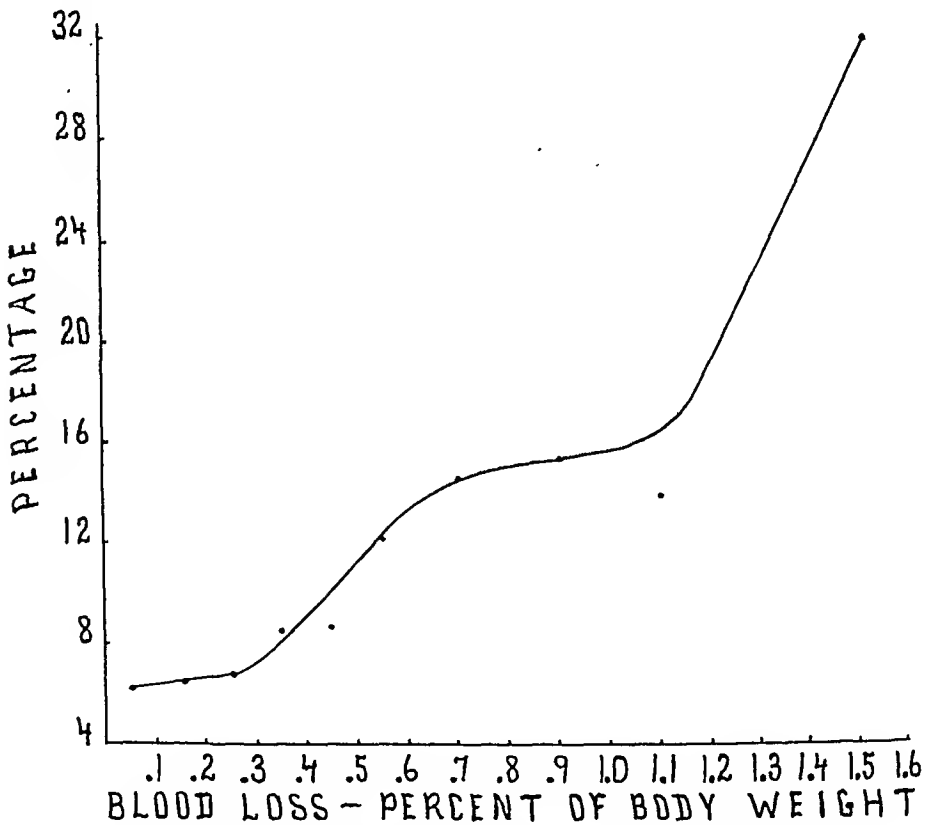


Fig. 1.—Showing relation of postpartum infection to the blood loss during the third stage of labor.

1.0 per cent blood loss, and increases the incidence to 31.8 per cent for an average blood loss of 1.5 per cent. This rise is represented as a straight line, although it should probably be a line parallel to the first rise. This is due to the fact that there were only 44 patients with a loss of over 1.1 per cent, and this number was too small to subdivide into individual groups.

It then became desirable to know if this increase in infection had any relation to the change in hemoglobin and cell volume following delivery, and if we could establish a method whereby we could predict the change in cell volume following a known blood loss. It had

been planned to follow the hemoglobin and the cell volume before delivery and during the puerperium. The Sahli method was used for the determination of hemoglobin, but in spite of the fact that all the determinations were done by me under controlled conditions, variations as high as 10 per cent were often noted on the same blood. This error is particularly noticeable when the determinations are made by different individuals, including students and internes. For clinical purposes it did not seem practicable to do the determinations by the oxygen method of Van Slyke. The studies have therefore been restricted to the cell volume determinations as outlined by Wintrobe. About 3 c.c. of blood were obtained by venipuncture, and to this two drops of heparin were added. To avoid congestion, the tourniquet was always removed before any of the blood was withdrawn. About 200 of the venipunctures were done by four members of the house staff of the Woman's Clinic, and the remaining 700 by me. All of the determinations were personally conducted. One cubic centimeter of blood was placed in a Wintrobe tube and centrifuged for one hour. The tubes were then allowed to stand for several minutes to regain room temperature, and the layer of white blood cells was disregarded in reading the cell volume. A total of 928 determinations were made.

The cell volume was studied before delivery and during the puerperium in 240 normal patients and in 48 with toxemia of pregnancy. In addition, cell volume studies of 31 other patients with antepartum toxemia, including vomiting of pregnancy, and cesarean sections, were made. Except for the cases of cesarean sections, the study of this small group was made only during the antenatal course. The third postpartum day was found most suitable for comparative studies, since the maximum drop in cell volume was usually attained by that day. The cell volume late in the puerperium was not constant because of the presence of infection in some of the patients. Most of the readings before delivery were obtained early in labor.

It was noticed in this investigation that the cases of toxemia, particularly those due to eclampsia and preeclampsia, deviated markedly from the normal course. Dieckmann in 1933 and Skajaa in 1929 made the same observation, although they did not correlate the changes with the blood loss. For this reason, in correlating the cell volume changes with the blood loss only the normal cases are considered.

Fig. 2 represents graphically the relation of the cell volume on the third postpartum day to the various groups of blood loss. The cell volume is expressed as a percentage of its value before delivery; for example, if the cell volume was 40 per cent before delivery and it dropped to 32 per cent on the third day, it was expressed as 80 per cent, indicating that there had been a 20 per cent drop in the cell volume. This method was employed in order to standardize all the changes. Obviously, comparison of absolute figures would be misleading, since all of the patients

did not have the same cell volume before delivery. It can be seen from the graph that the cell volume on the third day is higher than it was before delivery when the blood loss does not exceed 0.3 per cent. The graph is almost a straight line for losses up to 0.7 per cent. The cell volume change then remains constant between 0.7 per cent and 1.1 per cent blood loss. Beyond this range the drop in cell

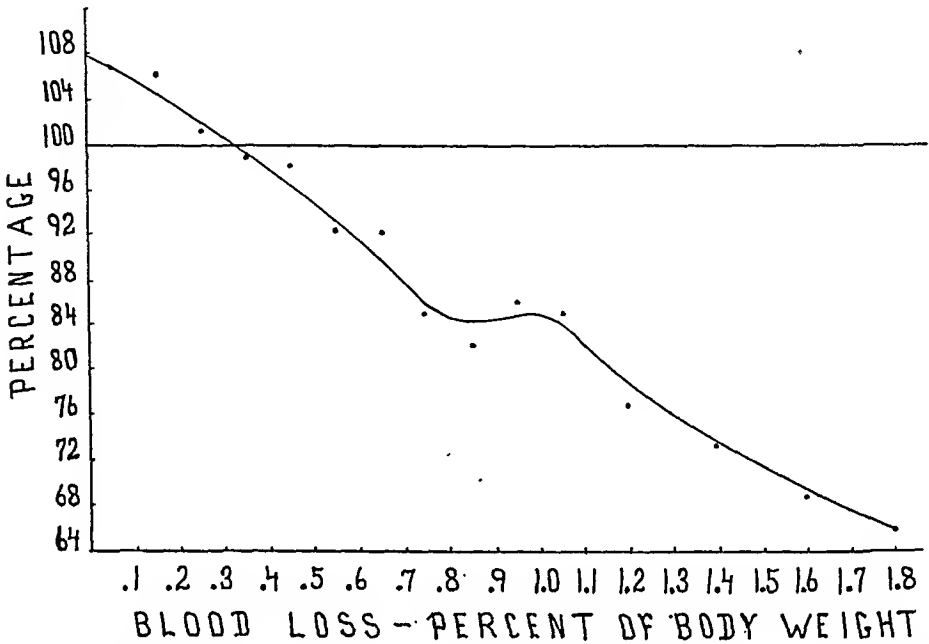


Fig. 2.—Showing relation of cell volume on the third postpartum day to the blood loss during the third stage of labor.

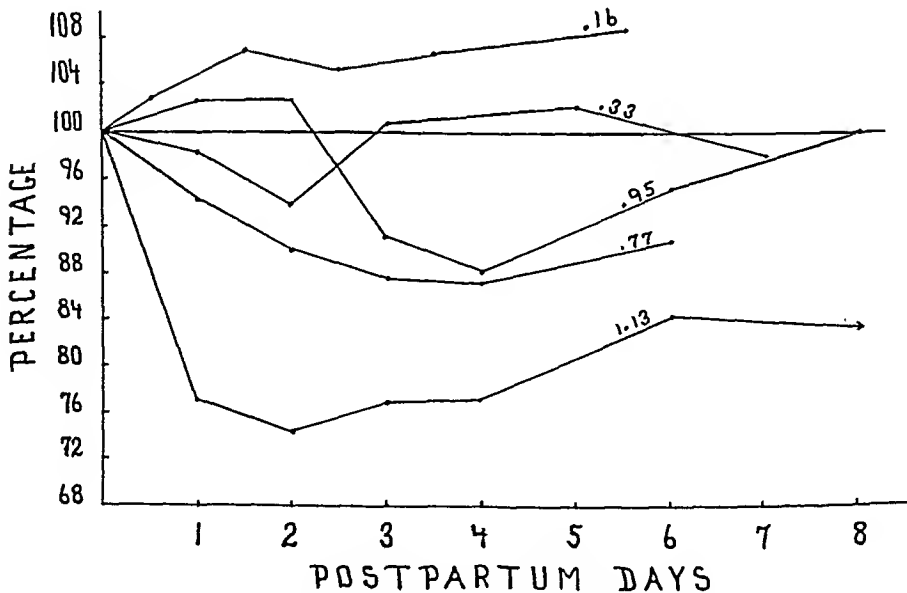


Fig. 3.—The course of the cell volume during the puerperium.

volume is almost parallel to the initial change. Here again the number of cases in the higher groups of blood loss is small. The range in cell volume, the average figure, and the number of cases in each group are given in Table I.

In Fig. 3 the course of the cell volume in the puerperium in 5 cases with different blood losses is represented. A discussion of these curves will be presented later.

DISCUSSION

The lowest incidence of postpartum infection is found in the group of patients with a blood loss of less than 0.3 per cent. In comparing Fig. 1 and Fig. 2, we find that within this range of blood loss there is an increase in cell volume by the third postpartum day. Such a rise in cell volume seems to be necessary for an ideal puerperium, since most of the patients who have an absolutely afebrile course, that is, with variations of not more than 0.2° C. above the normal, fall into this group of blood loss. With larger blood losses, in spite of the fact that the puerperium is considered afebrile, fluctuations in temperature

TABLE I. CELL VOLUME ON THE THIRD POSTPARTUM DAY WITH THE VARIOUS BLOOD LOSS GROUPS. CELL VOLUME IS EXPRESSED AS A PERCENTAGE OF THE VALUE BEFORE DELIVERY

PER CENT BLOOD LOSS	CASES	CELL VOLUME	
		RANGE	AVERAGE
Less than 0.1	27	99-119%	107.0%
0.1 to 0.2	44	92-121	106.3
0.2 to 0.3	36	87-113	101.2
0.3 to 0.4	40	89-108	99.0
0.4 to 0.5	19	80-110	98.2
0.5 to 0.6	18	80-108	92.1
0.6 to 0.7	16	77-100	91.3
0.7 to 0.8	12	83- 90	85.4
0.8 to 0.9	4	80- 86	82.0
0.9 to 1.0	9	72- 93	86.0
1.0 to 1.1	4	77- 94	85.4
1.1 to 1.3	4	69- 84	77.0
1.3 to 1.5	4	61- 81	73.6
1.5 to 1.7	3	62- 73	68.4
1.8	1		66.0

between 37° and 38° C. are usually noted. These we have been calling low-grade fevers although the temperature never reached 38° C.

This increase in cell volume must be due to dehydration of the blood following delivery, as has been recently shown by Oberst and Plass. Although an actual decrease in the total blood volume in the puerperium has not been clearly demonstrated, we do know, from the work of Plass and Bogert, Stander and Tyler, Stander and Creadick, Miller, Keith, and Rowntree, Dieckmann and Wegner, and many others, that there is dilution of the blood during pregnancy. Compensation for this dilution must occur after delivery or during labor. The amount of dehydration during the first three days of the puerperium is equivalent to 0.3 per cent of the body weight, since it is at this point that the dilution due to blood loss and the dehydration following delivery, are balanced. Furthermore, if this is true, we would expect that the drop in cell volume at 0.6 per cent blood loss should be the same as the rise at 0.0 per cent. From Fig. 2 it can be seen that this statement is correct, since the change in cell volume in each case is approximately 8 per cent.

Why should the incidence of infection between 0.7 and 1.1 per cent blood loss remain fairly constant? If there is any correlation between infection and cell volume, then the drop in cell volume within this range should also remain constant. Such a finding is demonstrated in Fig. 2. The only explanation which I can offer for this finding is that the bone marrow may perhaps be stimulated when the blood loss exceeds 0.7 per cent of the body weight. Apparently the maximum stimulation is obtained at 1.1 per cent since the drop in cell volume beyond this loss is parallel to the original drop. Although the blood from these patients was not studied for evidence of regeneration, we did note that the cell volume increased more rapidly in the cases with 0.9 per cent blood loss than in those with 0.7 per cent loss. Careful study of the blood and even of the bone marrow will be necessary to substantiate this conclusion.

In studying these cases on the basis of absolute values for the cell volume, it was found that in all patients who had a cell volume of 40 per cent or over on the third postpartum day, the incidence of infection was 4.5 per cent; in those who had a cell volume between 30 and 40 per cent, the incidence was 7.5 per cent and in those whose cell volume dropped below 30 per cent, the incidence of infection increased to 31.0 per cent. Furthermore, in the 19 cases of postpartum hemorrhage, which we have defined as a blood loss of 1.0 per cent or more of the body weight before delivery, there were 7 cases in which the cell volume was 30 per cent or over on the third day. Only one of these had a febrile course. In the other 12 cases the cell volume dropped below 30 per cent, and 6 or one-half of these patients had a febrile puerperium. The remaining 6 had a low-grade fever. The possibility that the low cell volume was due to the infection is ruled out, because the determinations were made at the time when the infection was nonexistent or just beginning. From this we can conclude that the absolute value of the cell volume is of importance.

What then should be our treatment in these cases? If the incidence of infection follows the cell volume curve, it would seem that our treatment should be directed toward maintaining as high a level of cell volume as is possible, not only during pregnancy but particularly after delivery. Medications are not useful after delivery since their action is slow. Transfusion is the only method which gives us a prompt replacement. Obviously we do not feel that transfusions are necessary in all cases of hemorrhage, since the incidence of infection in this group is only 31.8 per cent. The usual tendency is to "wait and see what the hemoglobin does." However, it is possible to determine at the time of delivery what the course of the cell volume will be during the puerperium. Knowing the cell volume before delivery and the blood loss in terms of the body weight, we can calculate, from the graph in Fig. 2, what the cell volume on the third postpartum day

will be. If we find that this calculated cell volume is below 30 per cent, then that patient should receive a transfusion within the first twelve hours following delivery. This is true not only for the cases with hemorrhage, but also for all patients with a blood loss above 0.3 per cent. The amount of blood that should be given depends on the weight of the patient, the blood loss, and the cell volume before delivery. In the average patient of 60 kg., a transfusion of 500 c.c. is equivalent to 0.83 per cent of the body weight. Purely from the standpoint of blood loss, if a patient lost 1.5 per cent and received 0.8 per cent in the form of a transfusion, the uncompensated blood loss would be around 0.7 per cent. By reference to Fig. 1, we would expect an incidence of infection of 14 per cent in contrast to 31.8 per cent, or a decrease of over 50 per cent in that group. If the transfusion were large enough so that the uncompensated blood loss was around 0.3 per cent, then the incidence of infection would approach the base line of 6.5 per cent. If the cell volume is also taken into consideration, we can go one step further. Knowing the cell volume before delivery, we can calculate, from the graph in Fig. 2, the amount of blood which that patient can lose before her cell volume drops below 30 per cent. If a transfusion of 500 c.c. is enough to replace the difference between the actual blood loss and the above calculated loss, then we could expect to maintain the cell volume above 30 per cent. According to the findings reported above, our expected incidence of infection would be 7.5 per cent. Moreover, if the transfusion was large enough to maintain the cell volume above 40 per cent, the incidence of infection would be around 4.5 per cent. The amount of blood necessary in each case can be calculated from Fig. 2. A more composite chart is not presented because this has not yet been tested clinically. I have of course not taken into consideration the stimulating effect of a transfusion, the difference in cell volume of the bloods of the donor and recipient, and the possible destruction of some of the red blood cells. Moreover the period of hospitalization for these patients has not been considered. We know from a previous study that patients with postpartum hemorrhage remain in the hospital on an average of three to four days longer than the normal cases. Such a treatment, therefore, would be economical for the hospital, especially if a free donor is secured.

Although this study was undertaken primarily to determine the changes in cell volume in the normal cases, I did have the opportunity of observing a few cases of toxemia of pregnancy. When the blood loss is expressed in terms of the body weight, variations from the normal can be easily detected. In the eclamptic and preeclamptic patients the cell volume dropped out of all proportion to the blood loss. On the basis of this study, this finding would explain the higher incidence of infection in this group of patients. Also during the acute stage of the disease there was a marked increase in the cell volume, as

was observed by Dieckmann and Skajaa. There was, therefore, dehydration of the blood in spite of the fact that there was excessive fluid in the body tissues. This seems to explain why so many of these patients have fever during the acute stage. Eden and more recently Peekham have shown that the presence of fever is a poor prognostic sign, and on this basis the fever would be an expression of the degree of dehydration occurring in the blood. In the true nephritic patients the cell volume did not drop as much as in the normal cases. Of the few cases of low reserve kidney which I observed, some behaved like the nephritic type, others like the eclamptic, and still others like the normal cases as far as the cell volume was concerned. In these cases of toxemia the cell volume must be an expression of the changes in the blood volume. This is substantiated by the fact that in the cases of vomiting of pregnancy the cell volume was markedly increased, and with subsequent improvement it returned to normal. It followed the curve of the CO_2 of the blood in the reverse order. It will be interesting to follow the cell volume in the cases of vomiting of pregnancy which do not improve with the usual treatment.

If the cell volume is a good index of changes in the blood volume, then we should determine the normal curve throughout pregnancy. It is not sufficient to know that the cell volume during the middle of pregnancy is lower than in the nonpregnant woman, or even at term. The normal curve of pregnancy, expressed in terms of percentage change, would be valuable in detecting early those cases which deviate from the normal, particularly the toxemias of pregnancy. Since eclampsia is associated only with pregnancy, it must be an expression of abnormal physiology, and until we know what the normal is, it will be difficult to determine the cause of the disease.

Another possibility along these lines is shown in Fig. 3, which represents the changes in cell volume during the puerperium in 5 cases with different blood losses. In two of these, 0.33 per cent and 0.95 per cent, variations during the first two days can be seen. Whether these changes are due to poor fluid intake and output or to some form of toxemia cannot be definitely stated at this time. Such changes were noted quite frequently during this investigation. In both of these cases the antenatal course and the puerperium were clinically normal.

Recently Dieckmann and Daily have stated that the measurement of the total volume of blood lost at the time of delivery is misleading because of the concentration or dehydration of the blood during labor. They recommended that the blood loss be calculated from the amount of hemoglobin lost. This involves the accurate determination of hemoglobin, by the oxygen method of Van Slyke, of the blood at the time of delivery and of the waste material on the drapes and floor. This method would be advisable if the concentration of the red blood cells were markedly increased. The slight difference in cell volume is more

than offset by the inability to collect all of the hemoglobin and also by the tremendous amount of work involved. In addition, such a method does not give any information regarding the blood loss during the three phases of the third stage or the course of the hemoglobin during the puerperium. These are of importance if we are to make any progress in the control and treatment of bleeding.

In this investigation the changes in cell volume during labor were usually slight, the marked changes occurring only in the cases of toxemia and of prolonged labor where dehydration was present. Moreover, if there is normal dehydration of the blood during labor it is only the beginning of the process which extends into the puerperium. If this is a constant finding, it should not interfere with the results which we are seeking, namely, Can the course of the patient during the puerperium be predicted at the time of delivery, so far as the cell volume and the possibility of infection are concerned? The preceding results have shown that this is possible if the weight of the patient, the cell volume early in labor, and the blood loss accurately measured are known.

CONCLUSIONS

1. The blood loss at the time of delivery should be expressed in terms of the body weight; that is, as a percentage of the weight before delivery. From a prognostic and comparative standpoint, this is much more valuable than the actual volume of blood lost.

2. On this basis a loss of 1.0 per cent or more is considered a postpartum hemorrhage.

3. The incidence of infection during the puerperium increases with an increase in blood loss. This increase varies with the blood loss as represented in Fig. 1.

4. The normal amount of dehydration of the blood during the first three days of the puerperium is equivalent to 0.3 per cent of the body weight.

5. The cell volume on the third postpartum day varies with the blood loss. It is higher than the value before delivery when the blood loss does not exceed 0.3 per cent of the body weight. With larger blood losses there is a drop in cell volume.

6. Stimulation of the bone marrow is probably obtained with losses greater than 0.7 per cent, with maximum stimulation at 1.1 per cent. This possibly accounts for the constant values in the incidence of infection and the change in cell volume within this range of blood loss.

7. The incidence of infection is also dependent on the cell volume on the third postpartum day. With a cell volume of less than 30 per cent, the incidence of infection is 31.0 per cent in contrast to 4.5 per cent when the cell volume is above 40 per cent.

8. The cell volume for the third postpartum day can be calculated at the time of delivery from the graph in Fig. 2. If this calculated cell volume is below 30 per cent, that patient should receive a transfusion within the first twelve hours following delivery. The amount of blood required depends on the weight of the patient, the blood loss, and the cell volume before delivery. This can also be calculated from Fig. 2.

9. In the toxemias of pregnancy the cell volume during the puerperium deviates from the normal course. The patients with eclampsia and preeclampsia have a greater drop in cell volume than is expected from the blood loss. The reverse is true in the nephritic patient. The low reserve kidney is not a pure type of toxemia as far as the cell volume is concerned.

10. The cell volume determination is a simple, accurate, and reliable procedure, and should be used more frequently in obstetrics.

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Bittmann, O.: The Justification of Special Anesthesia in Obstetrics, Monatschr. f. Geburtsh. u. Gynäk. 102: 223, 1936.

The advantages of spinal anesthesia for operative obstetrics are as follows: Absolute insensitivity of the field of operation, complete relaxation of the lower uterine segment, diminished blood loss as the result of the action of spinal anesthesia in the contractility and retractility of the uterus, absence of worry on the part of the operator, no alteration in the vitality of the newborn babies, subjectively favorable influence on the puerperium, especially on the involution of the uterus, and therapeutically good results in eclampsia because convulsions diminish.

Among the disadvantages the author mentions the drop in blood pressure, which may be serious, especially where there has been a great loss of blood. The danger of severe atonic hemorrhage after the effect of the spinal anesthetic wears off may be prevented by the prophylactic injections of pituitary extract and ergot. Pituitary extract perhaps also diminishes the severity of the headache which often follows spinal anesthesia:

TRAUMATIC GYNATRESIA

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VAGINAL and uterine packing, invaluable and often irreplaceable in the control of postpartum bleeding, cannot be employed indiscriminately with impunity. Unquestionably a life-saving measure in certain situations, it is neither innocuous nor free of sequelae. In four years we have seen five cases of irreparable vaginal atresia, each traceable, we believe, to a common etiologic factor; the packing of a lacerated, abraded vagina with iodoform gauze. In the same period we were twice forced to cesarean section in multiparas in whom we had anticipated easy, spontaneous delivery, by almost complete failure of cervical effacement and absolute default of dilatation of the external os. Again, a common etiologic agent was found; electrocoagulation of the endocervical mucosa for chronic endocervicitis.

The iodoform gauze used on our service is prepared by the resident nursing staff. In the preparation, under aseptic precautions, it is attempted to impregnate gauze packing with an emulsion of iodoform in glycerin. This is done manually and the usual product is entirely satisfactory. On occasion, an uneven distribution of iodoform occurs, often concentrated in palpable masses in the gauze, which may be the cause of actual burns of the vaginal mucosa. Such packing in the vagina abraded and lacerated by prolonged, traumatic delivery aggravates the already irritated area. When the packing is removed, the acutely inflamed mucosa, demonstrating early healing processes and possibly scattered bullae and blebs due to iodoform burns, collapses with the vaginal walls. The mucosae of the vaginal vault and floor and the lateral walls become contiguous. Sloughing at one area and healing at another may be concomitant and with ultimate healing, dense, fibrotic adhesions and areas suggestive of keloid formation unite the mucosae, producing atresia. Unfortunately this process occurs over the entire vaginal mucosa, and the atresia produced extends almost from the vulvovaginal orifice to the cervix. It is the distribution of the adhesive process throughout the vaginal canal that renders the resultant atresia resistant to treatment. Out of justice to the manufacturers of commercially available iodoform packing, it must be stated here that we have never seen atresia of any degree result from the usage of their packing; extensive experience indicates that there is no danger of atresia associated with properly prepared iodoform gauze. Where such is not available, it would be the course of wisdom to use plain packing

or, where the added advantage of antisepsis is desired, plain packing soaked in 4 per cent aqueous mercurochrome. This latter method was instituted on our service after the first four cases of atresia were encountered. A lapse in the procedure resulted in the fifth case. In the three-year period during which mercurochrome soaked packing was used no difficulty was seen.

The five cases, briefly described below, were seen in the postpartum clinic six to eight weeks following discharge from the hospital. Four of the five presented well-organized atresias at that time; dyspareunia was the chief complaint and with it vaginal bleeding following intercourse. No patient would accept hospitalization for treatment. The fifth patient had no complaint, the atresia being noted during the routine vaginal examination. She, too, refused therapy.

CASE 1.—M. M., para 0, colored, housewife, aged thirty-three, delivered with difficulty by Kielland forceps after prolonged arrest in midpelvis. Uterus and vagina were packed with iodoform gauze to control brisk postpartum bleeding. The perineum was intact. Birth weight of the baby was 8 pounds 8 ounces. The packing was removed forty-eight hours after delivery. She was discharged twelve days later in good condition. Delivery occurred on April 8, 1933. In the last week in May, vaginal atresia was observed at the postpartum clinic. Hospitalization was refused. On July 7, 1933, she returned complaining of dyspareunia, bleeding following coitus, and amenorrhea. In addition she stated that when she expected the period severe abdominal cramps had occurred and persisted three days. She was referred to the Gynecological Service where colpotomy was performed to relieve hematocolpos and hematometra. Dilatation of the vagina was attempted with glass dilators without satisfactory result. The patient signed herself out of the hospital and never returned for further treatment.

CASE 2.—J. O., aged thirty-two, colored, housewife, para iii, was admitted in active labor on March 23, 1932. Labor was rapid. A vertex presented and the interne on service had no difficulty delivering the head. Impaction of the shoulders occurred and ultimate delivery was effected by decapitation and cleidotomy (bilateral). Decapitation was deemed essential to permit proper and easier completion of the subsequent procedure. The stillborn child weighed 12 pounds 8 ounces. Uterus and vagina were packed with some 15 yards of iodoform gauze. Packing remained in situ for forty-eight hours. The patient had an uneventful puerperium and was discharged in good condition twelve days postpartum. In the first week in May, 1932, the examiner in the postpartum clinic noted the presence of an extensive atretic process in the vagina which prevented palpation of the cervix or fundus. On May 27 the patient was hospitalized complaining of dyspareunia, vaginal bleeding following coitus, and a persistent, bloody, vaginal discharge. The Gynecological Service attempted dilatation of the atresia with glass dilators but again prolonged treatment was refused.

CASE 3.—A. M., aged nineteen, white, unmarried. This patient delivered herself of a 7-pound 8-ounce stillborn child. After severe postpartum hemorrhage she was brought to the hospital by ambulance. On admission she was almost exsanguinated. The placenta was still within the uterus. After transfusion of 750 c.c. of whole blood, manual removal was performed, and the uterus and vagina were packed with iodoform gauze. Delivery took place on Nov. 13, 1932. In January, 1933 atresia was noted during routine postpartum examination. On March 30, 1933, the patient was hospitalized with the chief complaint of abdominal cramps and

dysmenorrhea. She was referred to the Gynecological Service where dilatation of the vagina was attempted with glass dilators, following manual dilatation of the vagina under anesthesia. She was discharged ten days postoperative and returned regularly for dilatation. On June 18, 1933, she was again hospitalized. The atresia had reestablished and the vagina was even narrower than on the occasion of the first admission. A plastic operative procedure was attempted with this admission, its purpose being to excise scar tissue and mobilize sufficient vaginal mucosa to recover the excised zones. The operative results were entirely unsatisfactory. The patient made several return visits for vaginal dilatation and then dropped out of the clinic.

CASE 4.—S. M., aged forty, colored, housewife, para iii, was delivered on Nov. 19, 1932, by Kielland forceps after failure of an occiput posterior to rotate anteriorly. A 9-pound 10-ounce baby was delivered. Profuse postpartum bleeding was controlled with iodoform packing of uterus and vagina. Packing was removed in forty-eight hours, and the patient was discharged in good condition ten days later. Twelve weeks following discharge she returned to the postpartum clinic where atresia was noted. At that time she was having a regular menstrual period. In December of 1933 she returned for examination. She was complaining of dyspareunia, amenorrhea, and severe, lower abdominal cramps. She noted that the cramps occurred only on the dates of expected menses. Vaginal examination was impossible, the atresia being present at the vulvovaginal orifice and extending to the cervix. Per rectum, a large, boggy, cystic mass was noted. She was referred to the Gynecological Service where colpotomy was performed to relieve the hematocolpos and hematometra. Postoperative dilatation of the atresia was attempted without success.

CASE 5.—J. C., aged thirty-nine years, colored, housewife, para xi, diabetic, delivered on Feb. 9, 1936. Transverse arrest occurred and delivery was effected with Kielland forceps. Impaction of the shoulders complicated delivery. An episiotomy was performed and a 12-pound 4-ounce baby delivered. Iodoform packing was placed in the uterus and vagina to control bleeding. The patient was discharged twelve days postpartum in excellent condition. On April 15, during routine postpartum examination, atresia of the vagina was noted. Vaginal examination was impossible since the atresia completely closed the vagina 1 cm. from the vulvovaginal orifice. The patient had no complaint. She was having a slight, bloody vaginal discharge. Inspection of the vagina revealed a complete closure of the orifice by what appeared to be normal mucosa. Close to the upper limit of the occluding membrane was an opening about 3 mm. in diameter through which the discharge could be seen escaping. She was referred to Gynecology where dilatation of the vagina was instituted.

Of these 5 patients, 2 complained of dyspareunia, 2 of dysmenorrhea, and 1 had no complaint. In 2, atresia was extensive enough to produce hematocolpos and hematometra. Therapy was eminently unsuccessful, and unless nature will permit gradual dilatation, these patients will never have functionally effective vaginas. The end-result in each of these cases favorably compares with similar results after expert management of the LeFort procedure.

In 1933, on two occasions, multiparas were admitted to the service in active labor; clinic cases, they had been thoroughly studied. Their prenatal courses had been normal, their pelves were ample, and from their histories and the adjudged size of the babies, no difficulty was anticipated. On admission, house men considered both fully dilated,

but it was noted that at no point, on rectal examination, was the margin of the cervix palpable. On vaginal examination, the presenting vertex was found to be covered by a smooth, elastic tissue presenting no opening. Inspection of the vagina with the speculum revealed a smooth, normal-appearing mucosa and no sign of cervix or external os. From the history of menstruation previous to pregnancy, we knew that a patent cervical canal must have been present. These 2 patients stated that they had been treated for profuse vaginal discharge by "burning out the neck of the womb." Records indicated that both had received electrocoagulation of the endocervix for chronic endocervicitis.

The bipolar electrode used in cervical coagulation is so constructed that, unless it is rotated while the current passes through it, coagulation will occur only at two points in the cervical canal. Where coagulation is performed with the electrode fixed in one position stenosis does not occur. Where the entire mucosa is destroyed at one sitting, slough and subsequent healing may completely close the canal or partially stenose it. Such stenosis is caused by the proliferation of dense, fibrous tissue which is undilatable. To prevent this accident one of two courses may be chosen. First, endocervical coagulation may be performed in two stages; second, after a one stage coagulation, or better, after any coagulation, uterine sounds should be gently passed through the cervix on several occasions and the patient should be instructed to report for examination after the first two menstrual periods have appeared. Dilatation gently performed with the sound will prevent stenosis, and unless the occluding pathology appears within two months, it will not appear.

These seven cases are presented to demonstrate the fact that dangers and associated sequelae are attached to apparently innocuous and beneficial procedures. The cure of endocervicitis is no justification for the risk of enforced cesarean section. Preventable iodoform burns of the vagina may be the starting point of prolonged physical, functional and psychic invalidism.

272 WEST 90TH STREET

509 WEST 155TH STREET

Robecchi, Emilio: Tubal Occlusion in Feminine Sterility, *Ginecologia* (Torino) 4: 463, 1936.

Based on the results of 180 hysterosalpingographies on women with primary or secondary sterility, the author stresses the high frequency of tubal occlusion in these patients.

Surgery offers very little assistance in reestablishing the patency of the tubes, but hysterosalpingography in itself occasionally causes occluded tubes to become patent and therefore proves useful at least in this respect.

AUGUST F. DARO.

PARENTAL AGE DIFFERENCE AND THE CONCEPTION OF CONGENITALLY MALFORMED CHILDREN

A STUDY OF 600 FAMILIES

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(From the Gyneccean Hospital Institute of Gynecologic Research and the Department of Obstetrics and Gynecology, University of Pennsylvania)

IN FAMILIES giving rise to congenitally malformed children, there is observed not infrequently a wide difference in the ages of the parents. In view of our lack of knowledge regarding the factors which may predispose to the production of congenital defects, the question is sometimes raised as to whether this parental age difference may not be an etiologic factor.

During an investigation of a consecutive series of families, each of which possessed a congenitally malformed child, the ages of both parents were ascertained. These figures with control observations are presented, since they appear to throw some light upon the problem under discussion.

MATERIALS AND METHODS

'To quote from a previous communication,* the material forming the basis for the present report was secured in the following manner:

There were found in the files of the Bureau of Vital Statistics, Department of Health of the State of Pennsylvania, 130,132 death certificates for stillborn and live-born individuals, who died in Philadelphia during the five years between Jan. 1, 1929 and Dec. 31, 1933. Each of these certificates was examined, and the data on those noting the existence of any congenital defect were transcribed to duplicate official forms; 1,476 such certificates were located.

The deceased individual was considered to have possessed a defect under either of two conditions: (1) If the defect involved the surface of the body, or (2) if internal, if its presence had been disclosed by either operation or necropsy. Diagnoses not conforming to these requirements were considered as not verified, and were excluded from further consideration. This reduced the total number of usable certificates to 890, or only 60 per cent of the original 1,476 certificates.

An attempt was made to interview the mother of each of the 890 deceased individuals, the visits being made in the summer of 1934 by three fourth-year medical students. A complete reproductive history was secured from each mother who could be located. The group forms a consecutive series. The defective children all died within a given geographic area and in a given period of time.

THE DATA

The ages of both parents were determined for a consecutive series of families in which 600 congenitally malformed children were born. These data are recorded

*Murphy, D. P., and Mazer, M.: J. A. M. A. 195: 849, 1925.

in Table I, with identical facts for 600 families, picked at random from the general population. The latter families were selected in the following manner: They were located through the medium of licenses on file in the Marriage License Bureau of the City of Philadelphia. The files of this Bureau for the years 1929 and 1933 inclusive, were inspected. The first 120 licenses issued during each of these years were examined, and the age differences of the applicants were noted. A few

TABLE I. AGE DIFFERENCE OF PARENTS

AGE DIFFERENCE IN YEARS	PARENTS			
	WITH DEFECTIVE CHILDREN		CONTROL	
	NUMBER	PER CENT	NUMBER	PER CENT
Reported	600	100.0	600	100.0
0-5	436	72.7	420	70.0
6-10	112	18.6	123	20.5
Over 10	52	8.7	57	9.5

substitutions were made in the resulting 600 records in order to insure numbers of control colored and white families comparable to the ones forming the defective child group.

It is evident from a glance at Table I that the distributions of parental age differences, in the defect families and in the control families, are essentially identical. On the basis of these observations, it is concluded that parental age difference is not a factor in the production of congenitally malformed children.

A CRITICAL ANALYSIS OF THE FIRST 3,060 CASES DELIVERED AT THE BRONX HOSPITAL*

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(From the Obstetric Service of The Bronx Hospital.)

THIS report representing 3,060 consecutive deliveries at the Bronx Hospital from July, 1932, through November, 1934, will add some proof to the theory that among the most important causes of the prevailing high mortality rate are unnecessary interference and lack of proper training of the obstetric attendant. One thousand of these cases are from the ward service and 2,060 from the private services. The class of patients cared for in the ward service varied from the extremely poor to the comfortable middle class. Most of these were Jews.

On the ward service the expectant mother is required to register with the antepartum clinic before the seventh month of gestation. She is seen at intervals of two weeks and in the last month of gravidity every week to the time of delivery. The antepartum care consists of a complete physical examination including blood pressure and urine examination, mensuration, hygienic and dietetic regulation. The appearance of signs of toxemia, blood dyscrasia and the like indicates more frequent observation in the regular clinic or a special clinic or, when necessary, hospitalization. During labor unnecessary examination and interference is eliminated, rectal examination instead of vaginal being used; and the work of the staff is carefully supervised. The private services observe a reasonable degree of proper prenatal care and no operations except low forceps can be done except under supervision.

*Read by invitation before the section of Obstetrics and Gynecology of the New York Academy of Medicine, January 28, 1936.

Of the 3,060 labors, operative delivery was done 730 times, a frequency of 23.9 per cent, with a neonatal and stillbirth mortality of 1.9 per cent for the total series and 9 per cent (58 in 730) for the operative cases; a maternal mortality of 0.3 per cent. It is of interest to note that of the 1,000 labors on the ward service, operative delivery was done 184 times, a frequency of 18.4 per cent with a neonatal and stillbirth mortality of 1.9 per cent for the total cases and 9.7 per cent for the operative cases and with only one maternal death (Table I).

On the private services the low forceps operation was done in the greater proportion of the cases as a prophylactic measure. If we deduct this group from the total operative incidence, there is an operative frequency of 14.1 per cent for the entire

TABLE I. OPERATIVE INCIDENCE, ENTIRE SERIES

OPERATION	TOTAL NO.		FREQUENCY PER CENT		MATERNAL DEATHS		INFANT DEATHS	
	WARD	PRIVATE	WARD	PRIVATE	WARD	PRIVATE	WARD	PRIVATE
Cesarean section	19	84	1.9	4.7		6	1	10
Low forceps	85	276	8.5	14.3			3	5
Midforceps	50	138	5.0	6.8	1	1	1	7
High forceps	1	3	0.1	0.1				2
Version	6	24	0.6	1.1			2	10
Breech extraction	18	26	2.1	3.9			6	9
Craniotomy	2	1					2	1
Totals	730		23.9%		8		59 = 1.9%	
Frequency for operative cases					1.1%		9%	

TABLE II A. VERSIONS

INDICATION	NO.	MORTALITY	
		MOTHER	BABY
Failure of forceps	10	0	4
Second of twins	9	0	5
Unengagement	6	0	1
Marginal previa	3	0	1
Transverse presentation	2	0	1
Totals	30	0	12

TABLE II B. BREECH

	NO.	MORTALITY		MACERATED	ANOMALIES	PREMATURE	ATELECTASIS	EXTRACTION
		MOTHER	BABY					
Spontaneous	69	0	2	2				
Extraction	44	0	15		3	1	1	10
Totals	113	0	17	2	3	1	1	10

series. Low forceps applications on the ward service were strictly limited to definite indications in the interest of mother or child. The greater number of low forceps operations was done in primigravida, the indications for which, in order of their frequency, were: (a) maternal distress and prolonged labor. (b) Fetal distress (character of fetal heart rate in addition to the mere appearance of meconium). (c) Cardiac complications. (d) Contracted outlet (rigid coccyx and outlet contractions in funnel pelvis).

The eight infant deaths in low forceps deliveries include two congenital anomalies, two neonatal deaths due to cerebral hemorrhage and four from unknown causes (all these cases were autopsied).

The 188 midforceps operations are divided into two groups: (a) head anterior at time of operation, 78, and (b) head in posterior or transverse arrest position, 110. The indications were strict and ran parallel to these for low forceps on the ward service.

There were two maternal deaths after forceps operations: (1) Hospital No. 37452, a primigravida who had a midforceps for fetal distress after 4½ hours of full dilatation, occiput anterior. She sustained a left cervical laceration which was re-

TABLE III. CESAREAN SECTIONS

INDICATION	NO.	TYPE OF OPERATION				MORTALITY	
		CLASSICAL	2 FLAP	LATZKO	PORRO	MOTHER	BABY
Contracted pelvis	60	20	33	5	2	4	2
Previous section	9	9					
Central placenta previa	8	8				2	2
Fetopelvic disproportion	7		1	6			1
"Ablatio"	6	3			3		6
Toxemia	3	3					
Complicating fibroids	3	2			1		
Cardiac disease	3	3					
Malposition	2		1	1			
Elective toxemia	2	2					
Totals	103	50	35	12	6	6	11

TABLE IV. POSTPARTUM HEMORRHAGE

CAUSE	NUMBER	TREATMENT	TRANSFUSION	MATERNAL DEATHS
Atony of uterus	3	Uterine packing	0	
Adherent placenta	1	Manual removal. Uterine packing	+	
Cervical lacerations	25	Cervical suture. Packing	+	1
Manual removal	1	Packing	+	

TABLE V. TOXEMIA OF PREGNANCY

TYPE	NUMBER	PREVIOUS TOXEMIA	DELIVERY		MATERNAL MORTALITY	BABY			
			SPONT.	OPERATIVE		PREMAT.	FULL TERM	LIVED	DIED
Eclampsia	1		1		0	1			1
Preeclampsia	12	1	9	3	0		12	12	
Nephritic toxemia	7		7		0	1	6	4	3
Unclassified	22		22		0	2	20	20	2
Total	42	1	39	3	0	4	38	36	6

Fetal Mortality 14%

paired. Cervix and vagina were packed and 1,000 c.c. of glucose infusion was given. After some time bleeding recurred and she died five and one-half hours after delivery after a further attempt to repair the cervix; and (2) Hospital No. 38209 in a primigravida who had a midforceps operation for ineffectual pains. Patient developed circulatory collapse and anuria and died in uremia four days later.

The eight infant deaths in the midforceps deliveries include six cases where the fetal heart was not heard before delivery; one baby that died of a bronchopneumonia ten days later; and one death due to cerebral hemorrhage.

The high forceps operation was done four times. In 1 case the patient had a borderline pelvis and an arrested O. T. Manual dilatation of a five-finger dilated cervix resulted in dislodgement of an engaged head, changing a midforceps to a high one. In the other 3 cases the operation was done for fetal distress on unengaged heads where versions were contraindicated. Two fetal deaths occurred in this group; one of these babies had a cerebral hemorrhage.

Internal podalic version and extraction was employed 30 times for the following indications: (a) failure of forceps in occiput posterior, 10; (b) second of twins, 9; (c) unengaged occiput with full dilatation, 6; (d) marginal placenta previa, 3; and (e) transverse presentation with prolapsed arm, 2. Here the fetal deaths included 5 premature babies (less than 3 pounds in weight); 4 full-term stillbirths after failure of Kielland forceps; 1 macerated fetus and 2 congenital anomalies (Table IIA) incompatible with life.

Breech presentation was encountered 113 times. The treatment was strictly conservative, allowing labor to proceed until the buttocks had passed through the vulvar orifice, from which point manual help by the operator completed the delivery. This we call spontaneous breech delivery. Any other procedure was termed a breech extraction. The latter was done 44 times, an incidence of 6 per cent in the entire series. In the spontaneous group there were two macerated fetuses. In the extraction group there were 15 fetal deaths: 3 anomalies, 1 premature, 1 neonatal death from partial atelectasis, and 10 deaths in all probability due to the extraction (Table IIB).

Cesarean section was resorted to 103 times, a frequency of 3.4 per cent. The indications were as follows: (a) contracted pelvis, 60; (b) previous sections, 9; (c) central placenta previa, 8; (d) fetopelvic disproportion, 7; (e) "ablatio," 6; (f) toxemia, 3; (g) complicating fibroids, 3; (h) cardiac disease, 3; (i) malposition, 2; (j) elective in toxemia, 2. All patients, except 5 in the previous section group, 6 in the "ablatio" group, and 3 in the cardiac group were allowed a trial labor. In all, the presenting part was unengaged at the time of operation. The classical operation was done 50 times, the two flap 33 times, the Latzko 12 times, and the Porro 6 times.

The Porro operation was done twice for placental apoplexy, once for an intrapartum infection, and the other three times for failure of uterus to contract following classical sections. One of these was complicated by intramural fibroids.

The Latzko procedure was done for potentially infected cases, with one fetal death and no maternal deaths. This has been reported elsewhere.

The six maternal deaths occurred as follows:

1. Hospital No. 35052. Primipara at term; central placenta previa; generally contracted pelvis. Classical section. Died on sixth postoperative day of sudden cardiac collapse. Stillbirth.

2. Hospital No. 40100. Primipara at term; central placenta previa. Classical section. Died on tenth postoperative day of peritonitis. Living baby.

3. Hospital No. 42845. Primipara at term; funnel pelvis, frank breech. Classical section. Died on sixth postoperative day from paralytic ileus. Living baby.

4. Hospital No. 43415. Primipara at term, contracted pelvis, nonengagement at end of twenty-four hours with membranes ruptured eight hours. Two flap section. Neonatal death. *Streptococcus hemolyticus* septicemia.

5. Hospital No. 44529. Primipara at term, flat rachitic pelvis. Intrapartum sepsis. Porro section. Autopsy: localized peritonitis. Living baby.

6. Hospital No. 47503. Primipara at term, flat pelvis, two flap section for nonengagement at end of thirty-six hours of ruptured membranes and eight hours of labor. Died of pneumonia. Living baby.

The 11 fetal deaths include 6 in mothers with ablatio (fetus already dead when section was done); 2 in mothers with placenta previa where fetal heart was lost be-

fore operation; 1 in a mother who died of the *Streptococcus hemolyticus* sepsis; 1 in a mother where a high forceps was attempted at home and later a Latzko section done in the interests of the mother, and one neonatal death from unknown causes (Table III).

Retained placenta occurred 18 times. All but three were removed manually within two hours after delivery because of continued bleeding. In three cases without bleeding the manual removal was done at the end of twenty-four to thirty hours because of a rise in maternal temperature.

Postpartum hemorrhage estimated at more than 500 c.c. followed the delivery of the placenta in 30 cases, which are grouped as in Table IV.

Included under the heading of toxemia of pregnancy (classification of Dr. Stander), are patients with symptoms of headache, dizziness, spots before the eyes, edema, as well as those symptom-free whose systolic blood pressure was above 140, or where albumin was present in the urine.

These cases are followed weekly in a special clinic where blood chemistry, kidney function tests, and eyeground examinations are made. They are seen postpartum by the same clinic personnel at the end of six weeks, one year, and two years, as to their ultimate outcome.

There were 42 cases of toxemia in the 1,000 ward cases. Because of lack of proper study the private cases are not included (Table V). More than 50 per cent of the cases fall into the so-called unclassified group which includes the low reserve kidney of Stander.

MATERNAL MORBIDITY

The standard of morbidity used in this group was a temperature of 100.4° F. (rectal temperature) on two occasions after the first day postpartum. There was a gross morbidity of 7.5 per cent. Among these there was a rise of temperature as a result of nonobstetric causes in 52 cases as follows: (a) upper respiratory infection, 30; (b) pyelitis, 14; (c) cholecystitis, 4; (d) acute thyroiditis, 1*; (e) toxic erythema, 3. This makes a net morbidity of 6.1 per cent.

MATERNAL MORTALITY

In this series of 3,060 cases there were 11 maternal deaths, a frequency of 0.3 per cent.

a. Hospital No. 37452. Primigravida who had a midforceps operation for fetal distress after four and one-half hours of full dilatation. In the extraction a left cervical laceration was sustained which was recognized and immediately repaired. Cervix and vagina were packed and a glucose infusion given. Bleeding recurred and she died five and one-half hours after delivery after a further attempt to repair the upper end of the cervical laceration and a transfusion.

b. Hospital No. 35052. Primipara at term; central placenta previa; generally contracted pelvis. Classical section. Died on sixth postoperative day of sudden cardiac collapse. Stillbirth.

c. Hospital No. 40100. Primipara at term; central placenta previa. Classical section. Died on tenth postoperative day of peritonitis. Living baby.

d. Hospital No. 42845. Primipara at term; funnel pelvis, frank breech. Classical section. Died on sixth postoperative day from paralytic ileus (probably peritonitis). Living baby.

e. Hospital No. 43415. Primipara at term, contracted pelvis, nonengagement at end of twenty-four hours with membranes ruptured eight hours. Two flap section. Neonatal death. *Streptococcus hemolyticus* septicemia.

f. Hospital No. 44529. Primipara at term, flat rachitic pelvis. Intrapartum sepsis. Porro section. Autopsy: localized peritonitis. Living baby.

g. Hospital No. 47503. Primipara at term, flat pelvis, two flap section for non-engagement at end of thirty-six hours of ruptured membranes and eight hours of labor. Died of pneumonia. Living baby.

h. Hospital No. 38209. Primigravida who had a midforceps operation done for ineffectual pains. Patient developed circulatory collapse and anuria and died in uremia.

i. Hospital No. 36582. Primigravida, normal spontaneous delivery, suddenly developed pulmonary edema thirty minutes prior to delivery and died shortly after.

j. Hospital No. 47100. Primigravida, normal spontaneous delivery, intrapartum influenza. Died of *B. influenza* sepsis.

k. Hospital No. 50532. Gravida iii, eclamptic, spontaneous delivery after Stroganoff treatment. Died twenty-one hours after onset of first convulsion.

INFANT MORTALITY

In this series there were 135 infant deaths, a mortality rate of 4.4 per cent, 32 were macerated fetuses and 8 were congenital anomalies, leaving a corrected mortality of 3.1 per cent. Of these, 51 were premature infants (i.e., less than three pounds), leaving a full-term corrected infant mortality of 1.4 per cent.

COMMENT

We have presented an analysis of a series of 3,000 cases treated conservatively; where the indications for operative intervention were carefully weighed. The only prophylactic form of obstetric procedure that was employed was the careful antepartum treatment accorded every patient and the closer watching and observation accorded to the particular patient showing abnormalities.

The use of the midforceps, as well as version and cesarean section for absolute indications only, resulted in an operative incidence of 23.9 per cent, a net maternal morbidity of 6.1 per cent, a maternal mortality of 0.3 per cent, and a corrected infant mortality of 3.1 per cent.

I wish to express my sincere thanks to Dr. Meyer Rosensohn, Attending Obstetrician at The Bronx Hospital, for his helpful suggestions and valuable criticisms in the preparation of this paper.

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215 EAST GUNHILL ROAD

Schumacher, P. H.: The Effect of Antithyroid Substances on the Secretion of Milk, *Monatsschr. f. Geburtsh. u. Gynäk.* 100: 211, 1935.

In August, 1934, Klüsterer reported that he had been able to increase the flow in lactating women by giving them antithyroid substance in the form of thyroxin. He based this therapy on his observation that a decrease in the amount of milk followed the administration of thyroid preparations. Schumacher tried to verify these results but failed. He did not observe any increase in the flow of milk after the use of antithyroid preparations. This author believes that the best way to obtain an increased secretion of milk still is complete emptying of the breast by the act of nursing or with the aid of a suction pump. However, he hopes that good results will soon be obtained with the use of the lactation hormone of the hypophysis.

J. P. GREENHILL.

INTERSTITIAL PREGNANCY*

CASE WITH EARLY RUPTURE, TREATED BY VAGINAL OPERATION

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THE interstitial portion of the uterine tube is the least common of all locations for the lodgment of tubal pregnancies. Based on the figures of Rosenthal and of Wynne, it appears to occur in no more than 1 or 2 per cent of all ectopic gestations.

The diagnosis of ectopic gestation at this site is almost impossible to make before rupture. Even after rupture it is seldom that it can be more than suspected of being in the uterine portion of the tube until exposed by operation.

The following case report is presented because of the comparative infrequency of the condition, the unusually early rupture in this instance, and the nature of the operation selected as being especially adapted to this type of case.

Mrs. M. C., a white woman, aged twenty-six years, married ten years, had three children, aged nine years, two and a half years, and eleven months, respectively. Each labor was spontaneous and the puerperia were uncomplicated.

Her last menstrual period began July 28, 1935 and ended Aug. 2, 1935, being normal in every respect. On Sept. 26, 1935, or seven weeks after her last period ended, the patient felt uncomfortable in her lower abdomen. Later, while working in her garden, she was suddenly seized with violent pain in the lower abdomen, became dizzy, and fainted. She recovered consciousness in not over five minutes and was able to crawl into the house but could not rise to her feet. After resting on the floor of her bathroom, she was able to rise and attempted ineffectually to defecate. She fainted again in the bathroom and was unconscious for approximately one hour. Finally, she was able to get to her bedroom and onto the bed, where her husband found her about two and one-half hours after the first attack. She was conscious at this time and refused to have a physician. There was no vaginal bleeding. At 9:00 P.M. she became unconscious again and a doctor was summoned who sent her to the hospital. The patient was admitted to the Pittsburgh Hospital at 10:00 P.M., semiconscious but in severe shock, with clammy skin and so weak a pulse that the rate could not be definitely determined. Her blood pressure was unreadable. The blood count disclosed 30 per cent hemoglobin and 1,900,000 red cells. The abdomen was distended and rigid and the vaginal examination was negative until the cervix was reached. This was lacerated, somewhat softened, and displaced anteriorly; slight movement of the cervix caused pain to the patient. The posterior fornix of the vagina was convex and bulging tensely. Uterus and adnexa could not be outlined. The diagnosis was ruptured ectopic gestation with severe hemorrhage.

The patient had been treated for shock by the usual methods and a 10 per cent aceaia solution (500 c.c.) had been administered intravenously. The blood pressure still could not be recorded; 500 c.c. of whole blood were then given by the Sorensen direct method followed by 1,000 c.c. of 10 per cent dextrose solution. Repeated attempts to read the blood pressure were made but no pulsation could be heard.

*Read before the Pittsburgh Obstetrical and Gynecological Society, April 6, 1936.

The patient's condition was so desperate that it was decided to attempt to clamp the bleeding vessels through the pelvic culdesae.

The patient was given nitrous oxide anesthesia, placed in a marked Trendelenburg position, the vagina prepared with iodine and a transverse incision approximately 2 cm. in length was made over the bulging area posterior to the cervix. When the peritoneum was opened, dark red blood and clots literally spurted out. The total amount was not determined. The index finger was introduced through the incision and the left adnexa was palpated. The tube and ovary on this side were normal in size and mobility. The right adnexa were next felt and also found to be normal but the right cornu of the uterus presented an opening into which the index finger could be introduced. It was now obvious that this was a ruptured interstitial pregnancy.

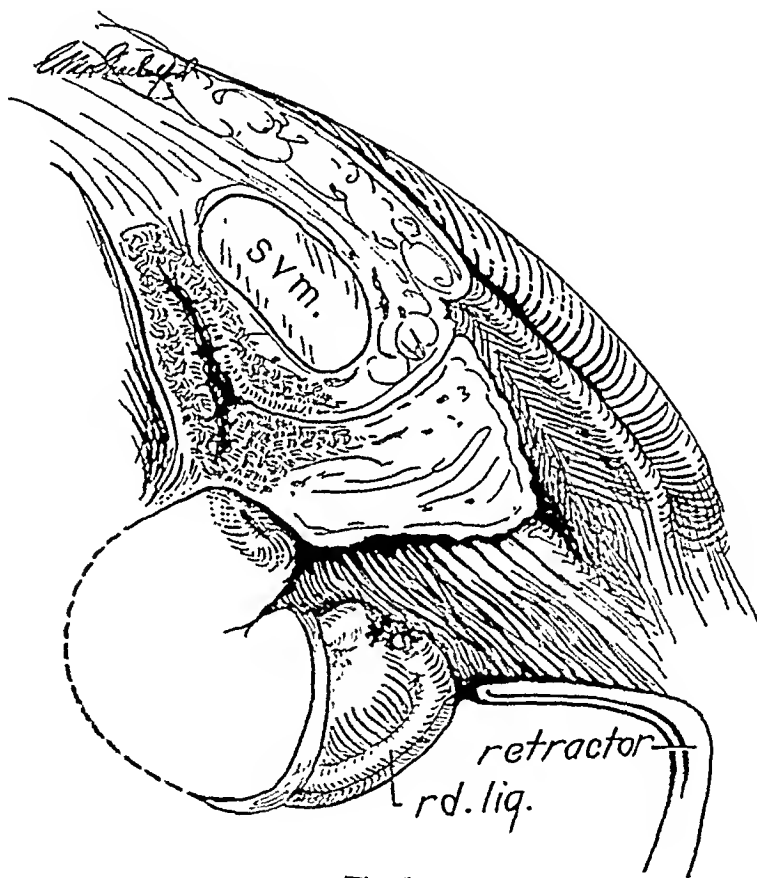


FIG. 1.

The uterus was displaced posteriorly and grasped with a tenaculum, the incision enlarged, and the uterus was drawn down and out through the vagina. The right cornu, approximately 1 cm. from the entrance of the tube, showed a horizontal tear about 2 cm. in length, the edges being very ragged, purple in color, and bleeding moderately. In the myometrium there were several grayish white areas which were removed for examination; fetal elements as such were not seen. The wound was quickly sutured, the uterus replaced, and three cigarette drains placed in the culdesac.

The time of anesthetic was twenty minutes and the time of operation twelve minutes.

During and following the operation, the patient was given 600 c.c. of whole blood and 1,500 c.c. of physiologic saline solution.

One-half hour after operation the blood pressure was 50, systolic, but the diastolic could not be determined. The pressure gradually rose until six hours later when it was 92/68, while the hemoglobin had become 50 per cent and the red blood cells had increased to 3,510,000.

The patient suffered a delirium on her second day and pulled out the drains. Subsequently she developed a pelvic abscess which necessitated reopening of the incision in the culdesac for drainage. She was discharged in good condition after sixty-one days in the hospital.

119 SOUTH HIGHLAND AVENUE

EPITHELIOMA OF THE CLITORIS

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PRIMARY carcinoma of the clitoris occurs very infrequently, but involvement of the clitoris in malignancy of the vulva is not unusual. It forms about 16 per cent of vulval cancers. From a study of reported cases, it appears that an average of 11.7 per cent of operative cases are free from recurrence for five years. Taussig's results after radical operation are the most encouraging.

M. G., sixty-three years of age, was admitted to the Kings County Hospital, on Oct. 29, 1932, with the following complaints:

1. Tumor mass protruding from the upper margin of the labia, painful and bleeding, after excessive activity.
2. Pruritus vulvae of long duration.
3. Progressive loss of weight and weakness.
4. Burning, frequent urination.

The previous history is essentially negative, except for pallor and palpitations. She had never borne any children.

For several years, the patient has had pruritus vulvae. In spite of all therapy, this has continued, with periods of exacerbation, and remission. About one year ago, she noticed a small nodule in the region of the clitoris. The family physician stated that the growth was then not malignant, and did not require removal. With an aggravation of the pruritus, and consequent scratching, the mass became swollen and painful. About six months previous to admission, she observed an increase in size, and slight bleeding after excessive walking. Since then there was a gradual loss of weight and weakness.

The patient was moderately obese, appeared chronically ill, pale and dyspneic on exertion. The relevant findings were: Heart sounds of poor muscular quality, normal rate and rhythm. Lungs normal throughout. No palpable masses, or points of tenderness in the abdomen. Inguinal lymph glands not enlarged, soft, discrete and freely movable on the underlying structures.

There was a "strawberry-like" ovoid pedunculated mass, deep red in color, involving the clitoris, about $1\frac{1}{2}$ inches long by $\frac{3}{4}$ inch wide, attached by a relatively thin pedicle. The lower margin of the pedicle was close to the urethra but did not involve it. Below this, involving almost the entire right labium minus, and the middle one-third of the left, there was a white, thick puckered hyperkeratotic area of leucoplakia. The vestibule was normal. The vaginal mucosa appeared uninvolved,

was senile and atrophic. The cervix was senile, the uterus small and atrophic, being smooth and symmetrical in contour, in second degree retroversion, and freely movable. The fornices were free from any induration or masses. No enlarged pelvic glands were palpable, nor could any masses be felt higher in the pelvis.

In view of the fact that the patient had a poor myocardium, and that her general condition did not safely permit the operation of choice, i.e. dissection of the superficial and deep lymph glands, followed by vulvectomy, it was considered sufficient to perform only a complete vulvectomy. Rather than to have a postoperative mortality, it appeared more rational to risk the treatment of any gland metastasis by deep x-ray therapy. On Nov. 23, 1932, under spinal anesthesia, an extensive complete vulvectomy was performed, removing all the tissues, down to the periosteum. Further exploration of the inguinal regions did not reveal any abnormal lymph glands.

The postoperative reaction was very poor, the temperature remaining elevated to 103°, because of infection of the wound (although drains were inserted at the operation, and there was sufficient drainage). The wound gradually healed, granulating in from below, the general condition of the patient was improved, and she was discharged with emphatic instructions to return for x-ray therapy in one month.

The patient did not return to the hospital until three months later. Examination at this time showed that the site of the operation was completely healed, there being no evidence of any local recurrence. In the left groin, just above Poupart's ligament, there was a metastatic nodule, about ½ inch in diameter, hard, not tender, and fixed to the underlying tissues. No other nodules were felt. Vaginally, the introitus was not stenosed; the urethral meatus appeared normal; no pelvic masses were palpable. X-ray study of the spinal column showed compression of the body of the first lumbar vertebra, suggestive of a metastatic new-growth. Hb 85 per cent, R.B.C. 4,288,000, W.B.C. 7,300, polys 64 per cent, lymph 36 per cent, blood chemistry normal. X-ray of the pelvis Apr. 13, 1933, showed metastasis to the pubic bone.

Between April 16 and May 4, 1933, the patient received a course of ten deep x-ray exposures to the inguinal regions, pelvis, and abdomen. On May 10, she was discharged and instructed to report to the out-patient department every month. Again she failed to return for four months.

On Aug. 21, 1933, she was admitted for the third time. The complaints were, pain in the left groin, radiating down to the thigh, and also in the lower spine, especially during change of posture and walking. There was considerable enlargement and matting together of the glands in the left inguinal region, the masses being firm and nodular. There was an area of fluctuation just above Poupart's ligament. The general condition of the patient was fair.

The pain gradually increased in severity, and it became necessary to incise the fluctuating area to relieve pressure. A small piece of granulation tissue was excised for diagnosis. The wound was infected, and drained a large amount of foul purulent material. This gradually decreased in amount, and the skin appeared to be healing. The patient was discharged on Oct. 10, 1933, and referred to the out-patient department for further care.

She was readmitted on Nov. 1, 1933, complaining of pain in the left groin and leg, a discharging gaping wound in the left inguinal region, and marked weakness. Blood examination showed: Hb 70 per cent, R.B.C. 3,040,000, W.B.C. 33,200, polys 79 per cent, lymph 21 per cent. Considerable loss of weight, marked pallor and asthenia were present. There were no additional signs or symptoms of metastasis to other organs. In the left groin, there was a discharging large open wound about four inches long by two inches deep. Surrounding this for some distance there was considerable induration. There was a profuse foul smelling,

purulent discharge. The edges of the wound were undermined, and it appeared excavated. On Nov. 11, 1933, there was a considerable hemorrhage from an eroded vessel. On November 24 the bleeding recurred. The wound was packed. Glucose was given intravenously and a transfusion was being arranged. The following morning, she again had a profuse, uncontrollable hemorrhage. In spite of all measures, she died November 25, one year after the original operation.

A NEW ALL METAL UMBILICAL CORD CLAMP*

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TO DICKINSON belongs the credit of being the first to point the way to the only certain means of preventing umbilical infections, even though his method of accomplishing it has not been adopted, namely, the complete removal of

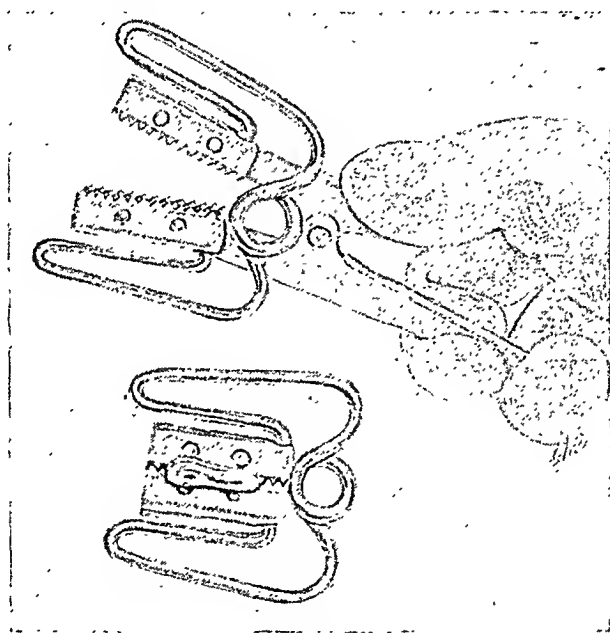


Fig. 1.

the cord stump. I have long been convinced of it, and over a period of more than fifteen years, I have been experimenting with numerous devices with the hope of duplicating Dickinson's results by nonsurgical measures. I believe that I have now accomplished it with the use of a new all-metal clamp which I have designed for the purpose. My first clamp, which has been quite generally adopted during the past twelve years, has given excellent results and has carried me a long way toward my goal which has been attained with the use of the new clamp.

The mechanism and operation of the new clamp are well illustrated by Fig. 1. The jaws are made of stainless steel, are an inch long and $\frac{3}{16}$ inch wide; the spring is made of vanadium-alloy steel and is chrome-plated. The peculiar design of the spring was found necessary to prevent fatigue of the metal, by distributing the tension placed upon it, and thereby preserve the resiliency and strength of the spring. The clamp is compact and is small, being less than $1\frac{5}{8}$ inch in diameter in either direction.

*Presented at a Meeting of the Pittsburgh Obstetrical and Gynecological Society, April 13, 1936.

On the compression surfaces of the clamp jaws are three rows of fine, sharp teeth which cut through the amnion, facilitating thereby the escape of moisture from the cord stump under pressure.

The clamp should be applied close to the skin margin. In applying it marked traction should be made on the cord in order to grasp the vessels as far down as possible and to include all of the amnion and jelly of Wharton, both of which end at the skin cuff, as you have seen on the screen in the microscopic section of the umbilicus of a newborn infant.

When the clamp has been applied, the retractor forceps should be removed and the stump cut close to the clamp jaws. A piece of gauze should be placed between

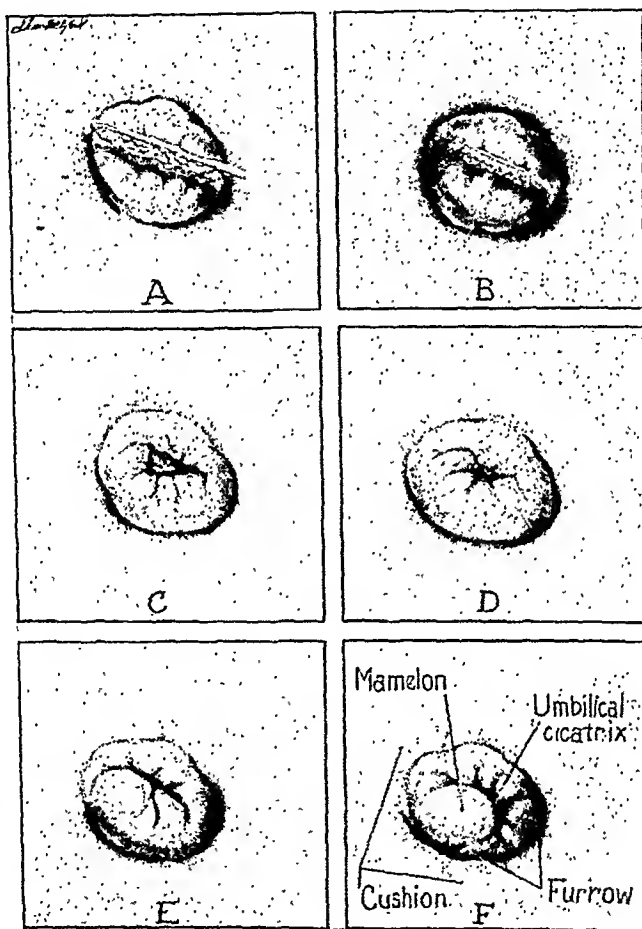


Fig. 2.

the clamp and the abdomen to absorb moisture squeezed from the stump. A binder should not be used. Instead, a piece of gauze bandage should be tied to one arm of the clamp spring, passed around the baby and attached to the opposite arm, to prevent traction upon the stump in handling the baby. Free exposure to the air hastens dehydration of the stump tissues.

In its operation the clamp rapidly produces complete dehydration of all the stump tissues within its grasp. The more powerful the spring, the sooner is the dehydrating process completed. Under the powerful and relentless pressure exerted upon the clamp jaws, the cord stump is compressed into a thin ribbon within a few minutes and in less than eight hours is reduced to a small, translucent, parchment-like film from which every trace of moisture has been removed. The walls of the blood vessels are so thoroughly fused that not a trace of them can be identified

in the film, under a magnifying glass. Secondary hemorrhage is thus impossible with this treatment of the stump and need not be further considered.

The clamp should be removed as soon as dehydration is complete, at any time between eight and twelve hours after birth, and the film trimmed as shown in Fig. 2 (B). Soon thereafter the skin margin of the umbilical ring begins to roll in as the result of the retraction and involution of the umbilical arteries. In forty-eight hours the new umbilicus is already well formed (Fig. 2, C).

All that is left of the cord stump after the film is trimmed is a small, adherent remnant of dried, pressure-necrosed cord tissue which aseptically and hermetically seals both the umbilical vessels and the umbilical ring. This necrosed tissue rapidly crumbles and separates as healing beneath it is completed; in less than a week there is nothing left of it. At no time after the clamp is removed is there an open wound and at no time is there any discharge or even moisture from the umbilicus. There is no visible scar such as follows healing of the granulating wound left when the stump is allowed to slough off. All that can be seen at the bottom of the umbilicus a week after birth are small punctate areas, the sites of the obliterated umbilical vessels.

Little further attention is needed after removal of the clamp. Binder and dressings are omitted. It is only necessary to keep the navel dry until healing is complete.

The drawings of the umbilicus from *A* to *E* (Fig. 2) were reproduced from photographs taken of the same baby at intervals of twelve hours, *A* and *B*; two and one-half days, *C*; four and one-half days, *D*; and *E*, eight and one-half days after birth, respectively. Drawing *F* is "Catteau's Scheme of the Adult Umbilicus" reproduced from Cullen's "The Umbilicus and Its Diseases" (p. 35), original drawing by Broedel.

Compare *F* with *E* taken just before the baby left the hospital.

MEDICAL ARTS BUILDING

Carvalho Azevedo, Fransisco de: The Problem of Voluntary Conception, Ann. Brasileiros de gynec. (Rio de Janeiro) 1: 255, 386, and 474, 1936.

In an article of 80 pages the author reviews exhaustively the work of Ogino and Knaus and the theory of the "safe period" as a means of contraception. He follows the dictates of Ogino in his recommendations to patients and publishes a convenient table to elucidate the periods of conception in women with all types of menstrual cycles from 21 to 45 days. He reports results of his use of Ogino's method in 50 patients who were personally directed by him over a period of three and a half years; he reproduces graphically the cycles of 19 of the 50 patients which had been followed for more than one year, and adds one other graph of a patient followed 8 months in whom the method failed.

A study of the graphs and a comparison of them with the author's table shows discrepancies between the reckoned periods of conception and the recommended periods of continence in 16, or 80 per cent, of the cases fully reported; the reason for these discrepancies is not clear. Despite this the author reports only two failures: one, the case mentioned above, whose cycles had been charted for only five months previously, and a second, in whom the method was employed after only two periods following an abortion.

To the reader who is interested in the theories of Ogino and Knaus this article offers a scholarly résumé of the literature; whereas to one interested in the clinical reporting of clinical results obtained, the article leaves a decided feeling of uncertainty as to the reliability of the "safe period."

THOMAS R. GOETHALS.

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

A BRIEF EPITOME OF GYNECOLOGIC ENDOCRINOLOGY AND ORGANOTHERAPY

EMIL NOVAK, M.D., BALTIMORE, MD.

THERE is much reason to believe that the general tone of gynecologic organotherapy has been very definitely raised within the past few years as a rather direct result of the gradual permeation of knowledge concerning, at least, the elements of female endocrinology. I have repeatedly urged that the way to teach organotherapy is to teach endocrinology. The salient points of the hormonology of reproduction, if presented to the average medical man in crystallized form, can be absorbed within a few moments. I do not mean that such tabloid teaching is the ideal method, but it will at least convince one that the subject is not quite so hopeless a muddle as some believe, and will enable one to evaluate the endless array of methods and commercial products directed toward the treatment of functional gynecologic disease.

It would probably be safe to assume that most of the readers of this JOURNAL have a working knowledge of the physiology of the female reproductive cycle, but, at the risk of triteness, a few cardinal points may be re-stressed. Just after menstruation a considerable group of follicles begins to mature, though as a rule only one during each cycle is destined to reach full maturation and to ovulate, usually at or near the middle of the intermenstrual period. These growing follicles produce increasing amounts of the follicle hormone, also called by many other names (estrin, estrone, folliculin, female sex hormone, theelin, etc.). This substance is demonstrable in both the blood and the urine by various tests. It occurs in many different forms, of marked degrees of potency, and is found, not only in the follicle, but also in many other body tissues and fluids (placenta, amniotic fluid, urine of pregnancy, etc.).

Moreover, substances of estrogenic type are found in many forms of plants and even minerals, so that this principle cannot be considered a specific hormone of the follicle. Nor does it represent just one substance, but a whole group of substances, and, in the present state of our knowledge, it is better to speak of the estrogenic substances rather than of the estrogenic hormone. This is particularly true since certain chemicals which are not hormones, such as some of the sterol group, are known to be estrogenic also. In spite of recent work purporting to identify one form of estrin as characteristic of the follicle itself, we cannot yet be sure on this point, or on many others concerning the life history of the estrogenic principle.

After the rupture of the follicle and the formation of the corpus luteum, the latter carries on the further production of estrin, so that this principle is present throughout the cycle. As might be expected, however, its amount in the blood drops quite abruptly with retrogression of the corpus luteum, which begins shortly before the onset of the succeeding period.

In addition to estrin, however, the corpus luteum produces a second and more characteristic hormone, progesterone, and this, so far as we know, is produced by no other tissue. It is probably not so sharply distinct from estrin as we formerly believed, for recent studies have shown a very close chemical kinship between the two. It seems not unlikely that progesterone is to be looked upon as only a modified estrin, just as the lutein cell is only a modified granulosa cell.

What are the effects produced by these two hormones? So far as the genital mucous membranes are concerned, and particularly the endometrium, estrin may be looked upon as a growth hormone possessing a remarkably specific effect upon the genital mucosa. It is responsible for the steadily increasing growth and hyperemia which characterize the endometrium from the end of one period to the beginning of the next. Progesterone, on the other hand, brings about the secretory and other changes which characterize the endometrium with the approach of the next menstrual period, changes which are apparently essential for the nidation of the egg if it happens to have been fertilized.

To bring these substances into the picture of chemical organotherapy, estrin is the principle which the clinician utilizes when he administers such commercial products as progynon, progynon B, theelin, or amniotin, in all their various forms. Another estrogenic substance, emmenin, prepared from the placenta by the method of Collip, has apparently been much less extensively used than those just mentioned. Progesterone, on the other hand, is the active principle of such commercial products as proluton, cor-lutin, lipo-lutin, etc.

Important as ovarian hormone function is in the menstrual cycle, it is not as fundamental as is that of the anterior lobe of the hypophysis, which dominates and makes possible ovarian function, as it does that of the thyroid and the adrenal cortex. Two sex hormones are produced by the anterior lobe. One of these, the follicle-ripening principle, is responsible for the maturation of ovarian follicles and thereby the production of estrin. The second, the luteinizing principle, is responsible for the conversion of granulosa and even thecal cells into lutein cells, and thereby the production of progesterone. Evidence is accumulating that these two pituitary sex principles are really separate hormones. It has not been possible to isolate them, although one or two commercial preparations purporting to contain them in at least impure form have been available for experimental clinical use (antuitrin of Parke, Davis & Co., gynantrin of Searle & Co., prephysin of Chappel).

Finally, there is a third pair of sex principles, obtainable from the urine of pregnant women, even in early stages. Indeed, it is upon their presence in the urine that we depend in the Aschheim-Zondek pregnancy test and its various modifications. Together these substances represent the composite called "prolan," consisting of two separate principles which on the ovaries of animals produce either follicle-ripening or luteinizing effects analogous to those produced by the pituitary sex hormones themselves. The evidence now seems quite clear that while these prolan principles of pregnancy urine are very "anterior pituitary-

like" in most respects, they differ in certain important points, and that they are not identical with the pituitary sex hormones themselves. They are therefore commonly spoken of as the anterior pituitary-like gonadotropic principles of pregnancy urine, or as the prolan substances. The follicle-ripening prolan principle is often spoken of as prolan A, the luteinizing, as prolan B. The latter at least is now quite generally considered to be not of pituitary, but of trophoblastic, origin.

It has not been possible to prepare these substances in separate form, but commercial preparations containing both, with apparently a predominance of the luteinizing principle, have been available for some years, and have achieved wide clinical application. The most generally used are antuitrin-S (Parke, Davis & Co.), follutein (Squibb & Co.), and antophysin (Winthrop Co.).

To summarize, therefore, the clinician anxious to practice organotherapy intelligently must know the rôle and significance of the two ovarian hormones, the two pituitary sex hormones, and the two anterior pituitary-like gonadotropic principles (prolan A and prolan B) of pregnancy urine.

Furthermore, he should know enough about the commercial preparations which he employs to be familiar with their hormone content, and he should select preparations made by manufacturers in whom he has confidence.

The other great essential for intelligent organotherapy is to know something of the nature of the endocrine disturbance involved in the functional disorders which he is so frequently called upon to treat, so that he may know what he is trying to accomplish with his treatment. Along many lines our knowledge is still meager and incomplete, but enough has been learned to enable the practitioner to distinguish the rational from the unsound in his attempts at treatment. It would scarcely be possible, within the limits of such a short review as this, to discuss all the endocrine factors which may be involved in the various functional gynecologic disorders which are so frequently encountered by the gynecologist, but it would seem that even a very brief epitome might be of service in differentiating the wheat from the chaff so far as organotherapy is concerned.

In the following discussion, references and citations from the literature are purposely omitted almost entirely, chiefly for the sake of brevity. This paper, in other words, is not a review of the vast literature on the subject, but represents simply what the author considers a sort of minimum working basis for the clinician who would like to treat his cases of functional gynecologic disease intelligently. For a fuller discussion of this and other aspects of endocrinology and organotherapy, as well as for a good working bibliography, the reader will find most useful the recently published volume on *Glandular Physiology and Therapy*, issued under the auspices of the Council on Pharmacy and Chemistry of the American Medical Association.

Amenorrhea.—It need scarcely be emphasized that the primary cause of many cases of amenorrhea, either primary or secondary, is not of endocrine nature, and that organotherapy is therefore not indicated. This applies particularly to such cases as constitutional debility, serious systemic diseases (anemia, tuberculosis, etc.), dietetic deficiencies, etc. When an endocrinopathy is the responsible factor, it most frequently involves (1) the anterior hypophysis and parahypophyseal areas of the midbrain, (2) the thyroid, and (3) the gonads. To say that we can

always differentiate these with precision would be incorrect, and yet it is possible to do so with reasonable certainty in many cases. While blood and urine hormone studies are often of help, the chief reliance must be placed upon careful clinical study, coupled with a familiarity with the characteristic features of each type. For example, the first of the three groups enumerated above is represented by the adipogenital dystrophy (Fröhlich syndrome) cases so commonly observed. In these the amenorrhea and other sex symptoms are due to deficiency of the pituitary sex hormones, while the characteristic obesity is now accepted as due to associated involvement of the hypothalamic and other centers in the vicinity of the anterior lobe.

In the treatment of cases of this type it would be rational to employ preparations of the pituitary sex hormones themselves, but, as stated above, the experience with the few preparations as yet available has not been sufficiently extensive or impressive to justify the statement that they are of much value. The oral administration of pituitary substances of one sort or another is believed by the best authorities to have little or no value, while the employment of the anterior pituitary-like gonadotropic principle of pregnancy urine has likewise proved unsuccessful, since the action of these substances upon the human ovary does not seem at all comparable to their effect upon the ovaries of certain laboratory animals.

Since the gonadal hypofunction in such cases is purely secondary to the pituitary disorder, the use of ovarian hormones is obviously purely substitutional. By giving large amounts of estrogenic substances (theelin, amniotin, or progynon B), for example 10,000 to 20,000 international units daily or every other day for from 6 to 10 doses, bleeding may in some cases occur, usually quite a number of days after the last injection. This, however, is not always the case by any means, and even when it does occur, the bleeding must be interpreted as due to retrogressive changes in an endometrium which has been artificially built up by the endocrine treatment.

Moreover, it must be remembered that such treatment leaves the ovaries untouched, that ovulation is not stimulated, and that, since there is no impetus to the ovarian mechanism, there is no reason to expect a regular recurrence of the bleeding, as in normal menstruation. For such reasons as this, and others which might be mentioned, ovarian therapy has been a disappointment in the treatment of amenorrhea, though, even if the physician is familiar with its limitations, its employment in certain cases is justifiable, as where the psychic effect upon the patient of producing even a spurious form of "menstruation" is an important consideration. In this connection, the physician can often fulfill a most important function by explaining the innocuousness of amenorrhea in itself, for there is no subject upon which wrong ideas are more prevalent than this.

In the great majority of cases of endocrinopathic amenorrhea, even if there is no obvious manifestation of thyroid deficiency, such as a low metabolic rate, the administration of thyroid substance, usually in the form of the dried extract, is advisable. Just what the mechanism of its effect may be no one seems to know, but it is much more likely to be beneficial than any other form of organotherapy. Where definite thyroid deficiency is evident, the rationale is much more clear, but even without this, a dosage of, in the average case, 1 to 1½ gr. of the dried

extract is not infrequently of much value. In the strikingly hypothyroid cases, the necessary dosage may be considerably larger.

What has been said with reference to the hypopituitary and thyroid cases applies also to the so-called primary hypogonadal cases. In some of these it would seem that the ovaries are really primarily at fault, as where the urine shows an abundance of pituitary sex hormones and an absence of estrin. In many, however, there is much less certainty on this point, and I believe that in not a few of these the ovaries would respond to the pituitary sex stimulation if the latter were forthcoming. The organotherapy of these cases does not differ materially from what has been detailed above, and the results are equally unimpressive.

In all types, the importance of such measures as exercise, general hygiene, and a properly balanced diet, should be impressed upon the patient. In a few cases, where the amenorrhea and the frequently associated obesity or sterility are extremely important problems, and where all other therapy has been unsuccessful, it seems permissible to resort to the tentative and very careful use of light radiation of the hypophysis or ovaries, or both. The procedure is manifestly semi-empiric, especially since there is no selective action of the rays upon any one group of cells. It is certainly not a plan of treatment which should be used frequently or without circumspection, though in our own experience we have noted no harmful results and have had good results in some cases.

Sterility.—Certainly a not inconsiderable group of cases of sterility are explainable on an endocrine basis, but unfortunately we know very little in most instances as to the endocrine factors involved. In some the sterility is associated with amenorrhea, so that the explanation and the treatment are identical with what has been said concerning the latter. Where there is definite evidence of hypothyroidism, thyroid therapy is clearly indicated. This is the most favorable group, so that the clinician is usually rather grateful when he receives a report that the basal metabolic rate is far below normal.

Another type of endocrinopathic sterility is represented by those patients in whom ovulation does not occur, even though menstruation is quite or nearly normal. These "anovulatory" cycles occur most frequently in very young women and those approaching middle life, though they may occur at any age. Their age incidence, in other words, is identical with that of the so-called functional bleeding, which likewise is associated with absence of ovulation and therefore sterility. Can anything be done to correct these? Unfortunately we do not know what endocrine factors are essential for ovulation, though the available evidence indicates that a certain quantitative balance between the two pituitary sex hormones determines the occurrence of the phenomenon. Since this balance differs in different species, and perhaps in different individuals of the same species, the problem of producing ovulation in the human being with our available knowledge and methods seems rather hopeless for the present. To rupture the follicles by bimanual pressure, as has been suggested by some, would not be altogether without hazard, and would probably not be successful, as it is doubtful whether, in the absence of the proper endocrine setting, the ovum would be capable of fertilization or whether follicle rupture would be followed by luteinization and corpus luteum formation. For the present the best plan, admittedly inadequate, seems to be to do everything possible to correct the constitutional and endocrine status of the patient, to give small doses of the inevitable thyroid, and

perhaps to administer the anterior pituitary-like hormones of pregnancy urine during the usual ovulation span, inasmuch as in animals at least these substances are capable of inducing ovulation.

In spite of the uncertainty as to the method of its action, thyroid therapy is quite generally believed to be much more frequently successful in the treatment of endocrine sterility than any other substance. It seems very likely, though there is no proof on this point, that its influence is exerted on the quality of the germ plasma. The doctrine of "defective germ plasma" as a cause either of sterility or habitual abortion is now accepted by the best and the most conservative embryologists, and it seems likely that this is the factor which may be influenced by thyroid treatment. The recent interest in the use of vitamin preparations, such as the germ-oil products, is evidently based on a supposed effect on similar lines, though, as a recent report of the Council of Pharmacy and Chemistry indicates, there is no reliable evidence on this point as yet.

Finally, in the consideration of endocrinopathic sterility, it should be emphasized that a search for endocrine factors in the husband is just as important as in the case of the wife.

Primary Dysmenorrhea.—There is no gynecologic disorder which calls for more thoroughness and individualization in its study than does primary dysmenorrhea. Many factors may enter into its causation, and treatment must therefore vary according to these factors. There is no doubt that some patients are improved by such general measures as exercise, improvement in general hygiene, proper diet, or hematinics when the blood examination indicates their use. It is just as certain that many cases are of psychogenic origin, and that they can be cured by psychotherapy, reassurance, and simple educational talks to the patient. Granting all this, however, there remains a rather large residuum of patients in whom none of these factors are demonstrable, and who seem intractable to any treatment, obtaining palliation only through the use of strong analgesics.

In some of these there is much reason to believe that the underlying cause is of endocrine nature, and that it consists of a qualitative imbalance between estrin and progesterone. The studies of Reynolds and others have demonstrated that in general the former is responsible for the normal, rhythmic activity of the uterine musculature, while progesterone is the normal inhibitor of this contractility. Incidentally, a similar inhibiting effect is exerted by the luteinizing or prolan B principle of pregnancy urine. It is on this basis that both progesterone and the prolan B principle have attained considerable vogue, following the suggestion originally made by Novak and Reynolds. When used indiscriminately or exclusively, the results are quite sure to be poor. When employed only with due regard to the elimination of other nonendocrine factors, much improvement will be noted in a considerable proportion of cases.

The usual plan for utilizing these preparations is to give daily intramuscular injections of 1 rat unit of progesterone or from 100 to 200 units of one of the pregnancy urine preparations daily, beginning usually three or four days before the menstrual period, and continuing until the flow is well established, when in the typical case the pain itself ceases spontaneously. The two preparations may be alternated or in very severe cases be used in conjunction with each other.

It should be added, and it is indicative of our organotherapeutic floundering in this field, that an exactly opposite plan has been advocated by some, estrogenic principles being used instead of those mentioned above. The biologic basis for this plan seems very unconvincing, and the results even more unimpressive than with the one I have detailed.

Habitual Abortion.—While the corpus luteum is apparently not so indispensable to the continuance of pregnancy in its early human stages, as it is in the case of such animals as the rabbit, there would seem to be no question that it is of considerable importance in these early stages, as it is in the preparation of the endometrium for nidation. In such a distressing condition as habitual abortion, intractable as it so often is to all other measures, it is not surprising, or irrational, that corpus luteum preparations have in the past few years gained wide popularity. Here again thorough study of the patient is necessary to rule out other possible factors, endocrine or anatomic. In most instances it is well to administer small doses of thyroid, even with a normal basal rate.

The use of progesterone preparations may be begun just as soon as the existence of pregnancy is definitely established. In most of the cases of this type reported in the literature, the dosage employed has been very small, much smaller than one would expect to suffice on the basis of physiologic work in animals. This conservatism has no doubt been in part due to the expensiveness of the preparations, though more recently they have become less costly. While the use of $\frac{1}{5}$ rabbit unit by intramuscular injection two or three times a week has seemed to be of service in many cases, it would seem that larger doses might be more effective, so that I have usually employed injections of 1 rat unit.

Functional Uterine Bleeding.—This very common menstrual disorder is often a most troublesome one to treat, especially in the case of young patients in whom preservation of the reproductive function is so important. When it affects women approaching middle life, the problem is usually much simpler, for, once the diagnosis is made, radiotherapy can be relied upon in practically all cases for permanent cure. In young women, however, even small doses of radium should be used as infrequently as possible and then with considerable caution, for fear of producing permanent injury of ovarian function.

It is now well established that the ovarian dysfunction concerned in this disorder consists of a failure of ovulation, with abnormal persistence of estrin stimulation and absence of progesterone effect, inasmuch as corpora lutea are not formed. The use of progesterone preparations, therefore, is rational, and has achieved wide popularity. Before progesterone was available for clinical use, the luteinizing principle of pregnancy urine, in the form of antuitrin-S, follutein or similar products, had been utilized for this purpose, with at least a fair measure of success.

When the progesterone preparations are employed, it seems best, when the bleeding is of menorrhagic type, to withhold them until the bleeding has commenced, or even for a few days beyond this, if the bleeding is not too severe. One rat unit may then be injected daily for from 1 to 6 doses, depending on the degree of response. In a considerable proportion the bleeding may be held down to almost normal limits, in others it is only moderately lessened, while in some there will be little or no improvement.

Where the patient suffers from persistent metrorrhagic bleeding, the organotherapy may be begun at once, also with daily injections. The

pregnancy urine preparations still seem to give better results in some instances than progesterone, so that, if the latter fails, 200 rat units of some such preparation as antuitrin-S or follutein may be tried. Or, the two preparations may be either alternated or used in combination.

Uncertain as this treatment is, no more effective organotherapy for this dysfunction is as yet known. In the occasional functional bleedings of definitely hypothyroid origin, thyroid extract is very effective, but these cases are the exceptions. In treating this disorder one is always justified in hoping for an endocrine readjustment to correct the underlying dysfunction, which is located in the pituitary. There is ample justification therefore in doing the best we can with our imperfect organotherapeutic armamentarium, so that the youthful patient may perhaps be tided over her stormy bleeding career until the hoped-for readjustment takes place.

Vasomotor Menopausal Symptoms.—While there is certainly no unanimity on the point, the prevailing viewpoint is that the withdrawal of estrin is the immediate factor in the precipitation of the characteristic vasomotor symptoms of the climacteric. Furthermore there is a rather general acceptance of the view that by far the most frequently effective means of lessening the severity of such symptoms consists in the administration of one or other of the various estrogenic preparations, such as theelin, amniotin, or progynon B. It need not be emphasized that only a minority of women need any organotherapy at all, and that other measures are often of great importance, such as the avoidance of stress and worry, the improvement of general health and hygiene, the use of simple nerve sedatives, etc.

It should be remembered, too, that the symptoms are usually very troublesome only in exacerbations, so that estrin therapy is not continuously indicated. When flushes and sweats come thick and fast, the injection of 1,000 international units, or even less, of the above-named substances every day or every other day, will often be followed by marked amelioration, though usually not complete relief of symptoms. This seems to be true even when cognizance is taken of the psychic effect of the injections. When such improvement occurs, the injections may be stopped, and perhaps small doses kept up by mouth. The oral method of administration is undoubtedly of value, though something like 5 times the hypodermic dose is necessary to produce the same effect. In the milder forms, however, it is likely to be less disagreeable than the hypodermic method, from 1 to 3 tablets or capsules of one of the readily available preparations being used, depending on the mildness or the severity of the symptoms.

Gonorrheal Vulvovaginitis of Children.—The plan of treatment of this troublesome disease which was suggested by Lewis in 1933, appears to have established itself as of genuine value. By building up the epithelial lining of the vagina by means of estrogenic substances, the duration of the infection is very definitely shortened. The vaginal mucosa of the immature child is very susceptible to the proliferative effects of estrogenic substances, so that it can be built up to a close simulation of the postpubertal vagina, which is notoriously resistant to the invasion of the gonococcus. When this method was first suggested, a number of misgivings were expressed as to possible harmful effects. Among these were the effects upon the breasts and the possibility of bringing on uterine bleeding. It is true that swelling of the breasts is occasionally noted, but it is transient, and disappears after cessation

of treatment. Bleeding is practically never evoked, and would likewise not be of serious significance.

The chief objection urged against the plan, however, was that it might, by evoking pelvic hyperemia, predispose to ascent of the gonorrheal infection into the internal genitalia. If one may judge from the literature, however, this objection is theoretical rather than real, so that the method seems to have been accepted as not only justifiable but of real value. Not a great many reports have as yet appeared in the literature, so that its final evaluation still remains for future experience to decide.

The dosage originally recommended by Lewis is 50 rat units hypodermically each day, this corresponding roughly to about 150 international units according to the newer methods of assay. More recently it has been shown that administration by the vaginal route is much more effective than by the hypodermic. This can be done by means of the daily insertion of the vaginal suppositories of estrogenic substances now available.

Senile Vaginitis.—This troublesome condition, occurring not infrequently in women following either a normal or surgical menopause, and associated with vaginal discharge, local irritation, and perhaps pruritus, is caused by infection superimposed upon the atrophic changes occurring after withdrawal of the ovarian secretion. The suggestion has been made (Davis) that the treatment with estrogenic hormone preparations may be effective in throwing off the infection by building up the atrophic mucosa. The results in the small series reported seem to have been favorable, though the treatment may have to be repeated from time to time if the symptoms recur. The dosage recommended is 75 to 100 rat units (about 225 to 500 international units) hypodermically three times a week, the duration of the treatment averaging six weeks.

Other Indications.—Ovarian therapy has been recommended for the condition of painful breasts or "mastoplasia," though its method of action is not clear and the results very uncertain. It is difficult to understand how estrogenic substances can be effective for a condition which many believe to be due to an excessive estrin effect upon the breast gland. Certainly the use of "ovarian residue" by mouth, a method recommended by one writer, has little to commend it, especially as the tablets of ovarian residue are generally accepted as almost or entirely inert.

The puzzling condition of menstrual edema, characterized by striking weight increase and often very obvious edema in association with the menstrual periods, is obviously due to a cyclical disturbance of the water-balance mechanism, though its mechanism is not known. Estrogenic therapy has been tried, and so has the use of the anterior pituitary-like principle of pregnancy urine, but usually without success. In at least one reported case, relief of the symptoms has seemed to follow employment of emmenin (Collip), an estrogenic substance prepared from the placenta and said to be active when given by mouth.

Still other indications might be mentioned, such as menstrual headaches and acne vulgaris, in both of which improvement is said by different observers to have followed the use of estrogenic substances or the pregnancy urine products. So little is known of the hormonal relations of these conditions, and so poorly defined are the results, that there would not seem to be any advantage in discussing them at length.

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

MATERNAL MORTALITY STUDY FOR AKRON, OHIO

GEORGE A. PALMER, M.D., AKRON, OHIO

THIS report is a study in which each hospital maternal death occurring in Akron, Ohio, during the past two years has been individually studied and classified according to the classification adopted by the Hospital Obstetric Society of Ohio. The chief of the obstetric department of the various hospitals is responsible for the presentation of all case histories and pertinent facts of each maternal death occurring in the respective hospitals. Regular quarterly meetings are held by the members of the Society from the various approved hospitals at which time all cases are presented, discussed, classified, and recommendations made whenever necessary, of all deaths occurring in the preceding three months. With all facts at hand, this seems to me to be a most accurate manner of determining the true etiology of all hospital maternal deaths and for any recommendations that will subsequently reduce our maternal mortality.

During the year 1934 there were 4,318 live and stillbirths in the city of Akron. Of this number 1,980 occurred in the hospital. There were 25 maternal deaths which occurred in the hospital. Of the 25 cases only 9 were supposedly normal on entrance to the hospital, and 16 were admitted with known pathology. The 9 patients who died, that were supposedly normal on entrance, include: 2 nonseptic emboli following full-term delivery; 2 septicemia following full-term delivery; 2 hemorrhage: (a) postpartum following full-term delivery, and (b) following cesarean section for placenta previa; 1 peritonitis following cesarean section; 1 septicemia following cesarean section; 1 shock, full-term delivery, placenta previa.

There were 4 of these 9 deaths which were classified as possible hospital origin: the 2 cases of septicemia following full-term delivery, the case of septicemia following cesarean section, and the case of peritonitis following cesarean section.

The patients admitted to the hospital with known pathology include: 6 septic abortions; 4 ectopics (ruptured); 1 septicemia following home delivery; 2 cardiacs: (a) death following cesarean section (noninfectious), and (b) late toxemia (noninfectious); 2 toxemias: (a) hydatidiform mole (noninfectious), and (b) cerebral hemorrhage (noninfectious); 1 pernicious anemia, full-term delivery (noninfectious). Five of the above cases were classified as noninfectious.

During the year 1935 there were 4,164 live and stillbirths in the city. Of this number 2,276 occurred in the hospital. This is a decided increase in the number of hospital deliveries over the year 1934. Also the number of hospital deliveries exceeded the number of home deliveries during the year. There were 25 maternal deaths which occurred in the hospitals. Of the 25 patients only 3 were supposedly normal on entrance to the hospital, leaving 22 which were admitted to the hospital with known pathology. The 3 patients who died that were supposedly normal on entrance include: 2 peritonitis following full-term delivery; 1 shock, full-term delivery, breech, anencephalic monster. The 22 patients admitted to the hospital with known pathology include: 8 septic abortions; 1 ectopic (ruptured); 4 sep-

ticemia following home delivery; 2 peritonitis following home delivery; 2 bronchopneumonia: (a) following influenza, home delivery, and (b) death before viability; 1 myocardial failure, thyrotoxicosis, seven month's pregnancy (noninfectious); 1

TABLE I

	PREG. AND LABOR NOTING TO DO WITH DEATH	PREG. AND LABOR NOT PRIMARY	PREG. AND LABOR PLUS CONTRIBUTORY	DEATHS BEFORE VIABILITY	NONINFECTIOUS	EXTRA HOSPITAL ORIGIN	POSSIBLE HOSPITAL ORIGIN	KNOWN PATHOLOGY ON ENTRANCE	SUPPOSEDLY NORMAL ON ENTRANCE	HOME DELIVERY HOSPITAL DEATH	NONRESIDENT	POSTMORTEM
1934	0	1	1	10	10	1	4	16	9	1	1	8
1935	1	4	2	10	7	8	2	22	3	8	2	12
Total	1	5	3	20	17	9	6	38	12	9	3	10

TABLE II

	ABORTIONS	ECTOPICS	LATE TOXEMIA	CARDIAC	HEMORRHAGE	SHOCK	NONSEPTIC EMBOLUS	ANTEPARTUM PNEUMONIA	POSTPARTUM INFECTION	OTHER CAUSES	TOTAL DEATHS
1934	6	4	1	2	2	1	2	0	5	2	25
1935	8	1	2	0	1	1	0	2	8	2	25
Total	14	5	3	2	3	2	2	2	13	4	50
Per cent	28	10	6	4	6	4	4	4	26	8	

TABLE III

	HOSPITAL	LIVEBIRTHS	STILLBIRTHS	TOTAL BIRTHS	MATERNAL DEATHS	SUPPOSEDLY NORMAL ON ENTRANCE	PER CENT NORMAL	KNOWN PATHOLOGY ON ENTRANCE	PER CENT PATHOLOGY	HOME DELIVERY HOSPITAL DEATH	DEATH RATE TOTAL BIRTHS	DEATH RATE VIABLE BIRTHS	DEATH RATE POTENTIALLY VIABLE BIRTHS	ABORTIONS	PER CENT ABORTIONS
A	1934	958	37	995	13	3	23	10	77	1				3	
A	1935	1,118	32	1,150	12	1	8	11	92	3				5	
A	Total	2,076	69	2,145	25	4	16	21	84	4	1.16	1.20	0.62	8	32
B	1934	436	10	446	6	3	50	3	50	0				2	
B	1935	570	15	585	5	0	0	5	100	2				12	
B	Total	1,006	25	1,031	11	3	28	8	72	2	1.06	1.09	0.49	4	36
C	1934	526	13	534	6	3	50	3	50	0				1	
C	1935	515	26	541	8	2	25	6	75	3				1	
C	Total	1,041	39	1,080	14	5	35	9	65	3	1.29	1.34	0.86	2	21
Grand total		4,123	133	4,256	50	12	24	38	76	9	1.17	1.21	0.65	14	28

eclampsia following home delivery (noninfectious); 1 acute hemorrhagic nephritis (noninfectious); 1 nephritic toxemia, full term (noninfectious); 1 premature separation of placenta, cesarean section, seven months' second-degree burns of back and thighs (noninfectious). Five of the above cases were classified as non-infectious.

The above data for both the years 1934 and 1935 are classified in Tables I and II. There are additional headings on the classifications adopted by the Society, but inasmuch as there were no cases in this particular study of those types, the additional headings were omitted.

DISCUSSION

Of the total number of deaths for the two-year period, 38, or 76 per cent, had known pathology on entrance to the hospital. Only 12 cases, or 18 per cent, were supposedly normal on entrance to the hospital. Just 6 cases, or 12 per cent, were classified as possible hospital origin. This rather speaks for the safety of hospital as compared with home delivery. This report definitely indicates that the hospitals have been unjustly credited with maternal deaths that rightfully do not belong to them. I feel that comparable studies made throughout the country will show a similar condition to exist. The death rate, based on all births, is 1.17 per cent, while the rate based on only the potentially viable births is 0.65 per cent. The figures on abortion as a cause of death are quite astounding. When we consider that 14 or 28 per cent of the total number of deaths are due to abortion, we should be cognizant of the fact that it is time for the medical profession to swing into action to remedy this situation. The patients who died as a result of shock, hemorrhage, and postpartum infection are the type of case in which we have great hopes that this Society and similar organizations will be effective in reducing this mortality to a decidedly lower figure.

SUMMARY

1. Seventy-six per cent of all patients dying in the hospital were admitted to the hospital with known pathology on entrance.
2. Only 12 per cent of the total deaths can be attributed to possible hospital origin.
3. Deaths as a result of abortion accounted for 28 per cent of the total number of deaths.
4. Nine of the deaths attributed to the hospital were patients who were delivered in the home and subsequently sent into the hospital.
5. The death rate based on potentially viable births is 0.65 per 1000.
6. Similar accurate analytical and statistical studies should be made in other localities to determine the true etiologic factors responsible for our high maternal mortality.
7. Patients dying as a result of hemorrhage, shock, postpartum infection, and abortion as described in this report, are the type of cases which the medical profession can, by proper control, eliminate for the most part, thus reducing our all too high maternal mortality in this country.

American Journal of Obstetrics and Gynecology

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Editorial Comment

THE relief of pain in childbirth ever has been the objective of obstetricians but practical success has only been attained in more recent times. Many anesthetics and hypnotics have been tried and recommended for the production of analgesia and amnesia in labor. It is clear that every drug producing these effects must not only alleviate the mother's discomfort but must not jeopardize the safety of the child. Every analgesic used in labor should, therefore, be scrupulously studied as to its effects on both the maternal and fetal organism. This applies in particular to barbituric acid derivatives, for these substances have in the past few years gained preeminence as obstetric analgesics.

The data concerning the action of barbiturates on the several functions and organs of the body are abundant, while the effect of these drugs on the fetus has not been studied adequately. It was only quite recently that information on this subject became available, partly clinical and partly experimental in nature.

Fabre administered to one pregnant dog a daily dose of 0.5 gm. of barbital by mouth for five days before delivery, and reported the discovery of diethylbarbituric acid in the fetus. Boneek and Renton, on the other hand, gave amytal to pregnant rats near term and tested the viability of the fetuses by mechanical stimulation. They observed that there was no depression of the fetuses when amytal was administered to the mother, and hence concluded that the placenta is not permeable to amytal. We have, then, two conflicting reports on the permeability of the placenta to barbiturates.

More recently Koppanyi's methods on the extraction and quantitative determination of barbiturates made it possible to study this subject in an exact and quantitative manner. Working in Koppanyi's laboratory and using his methods Dille found that the placenta presented no barrier to the passage of either barbital or amytal. The fetus in taking up the barbiturate from the blood of the adult body behaves like an organ of the adult body, the barbiturate reaching a

maximum concentration rapidly in the fetus with a fall in the concentration of the barbiturate in the maternal blood. The concentration of the barbiturate may reach a fairly high level in the fetus. In some cases this concentration approaches and reaches anesthetic levels.

Dille's earlier results were obtained with the injection of *full anesthetic* doses of barbiturates, and the objection was raised that in the obstetric practice such doses were not employed. To meet this objection he performed a series of experiments using only hypnotic doses of barbital in pregnant rabbits near delivery, and found not only that barbital is transmitted through the placenta even in *hypnotic* doses, but also that the concentrations of barbital in the fetus are directly proportional to the size of the dose administered to the mother.

The clinical studies on the effect of barbiturates on the offspring did not yield uniform or conclusive results. To quote only a few investigations: Morehead and Mussey reported no ill effects on the offspring with small doses of amytal given to the mother by mouth. With larger doses Swendson observed that about one-third of the babies were somewhat apneic at birth, and Shir and Daichman reported that following the use of barbiturates in labor the babies were frequently narcotized.

The conflicting clinical results are obviously due to the size of the dose of barbiturates used during labor. It is not to be expected that the fetus will show lesser effects from the drug than the mother. Dille's investigations have proved beyond any doubt that the barbiturates permeate the placenta, and the concentration of barbiturates in the fetus depends upon the size of the dose given to the mother. Entirely aside from the dangers to the mother which may result in administering a fixed anesthetic, the barbiturates present definite hazards to the child and to the course of labor. It is very important and essential therefore that greater care be exercised in their administration. In addition, the frequently observed prolongation of labor associated with the employment of analgesic preparations must have an important bearing on stillbirth and maternal mortality rates.

Kraus, E. J.: The Pathogenesis of Galactorrhea, Arch. f. Gynäk. 155: 380, 1935.

The proliferation and hypertrophy of the milk ducts during pregnancy is the result of stimulation by the ovarian hormones. The lactation hormone is probably a product of the pregnancy cells which cannot be activated until the placental influence has been removed.

The author describes two instances of galactorrhea in nulliparas both of whom showed some degree of hyperpituitarism. Both had hyperplasia of the eosinophiles of the anterior lobe with proliferation of the hypertrophic main cells. In both, the ovaries were degenerated. These changes in the pituitary were due to pressure, one following a tumor of the third ventricle and the other a tumor of the sella turcica.

RALPH A. REIS.

Correspondence

August 19, 1936.

To the Editor:

There are several statements in Dr. Kanter's article (AM. J. OBST. & GYNEC. 32: 183, August, 1936) on fibroids in which reference is made to my publications on the same subject. Perhaps further discussion of these statements will tend to establish our respective positions and will clarify the subject matter for the reader in general.

In *Surgery, Gynecology and Obstetrics* (61:743-750, 1935), I made the statement, "The hypothesis that all forms of overgrowth of the uterine endometrium or musculature are due to the same factor, the estrogenic principle, is not only supported by clinical and pathologic data, but also explains satisfactorily the simultaneous development of endometrial hyperplasia, endometriomas and uterine fibroids, with their associated clinical features, hemorrhage and sterility." From a study of 100 cases of uterine fibroids, Dr. Kanter undertakes to evaluate this theory.

Dr. Kanter brings up the point, and a very true one indeed, of the infrequency of endometriosis in the colored woman with fibroids. He states: "Witherspoon further deduces that the same etiologic factors (the estrogenic principle) are active in producing adenomyosis, a condition that was relatively rare in our colored patients but *common in the white woman who had no evidences of pelvic inflammatory disease* [*italics mine*]. This becomes increasingly difficult to understand since the colored woman had, as a rule, larger tumors, a fact that would suggest a greater excess in the circulating estrin content." The infrequency of endometriosis in colored women with fibroids is a well-known clinical fact, but there is, to me, a rational explanation for the rarity of its occurrence in this race, namely, the high incidence of salpingitis, with resulting occluded tubes. Retrograde menstruation with peritoneal, ovarian, etc., inoculations with uterine endometrium cannot occur through a blocked tube; hence the infrequency of endometriosis in the colored woman. Conversely, the high incidence of endometriosis in the white woman with fibroids (64 per cent in my series) can be explained on the same basis, the relative lack of salpingitis in the Caucasian, with resulting opportunity for retrograde menstrual endometrial implants to occur through patent tubes. Of course, complete belief in metaplasia-of-serosal-cells origin of endometriosis discredits this explanation.

Another point which Dr. Kanter mentions is, "If hyperplasia of the endometrium can be taken as a criterion of excessive estrin stimulation, one would expect to find more than a 53 per cent (his figure) incidence in a series of patients with fibroids." Cannot this apparent discrepancy with the original hypothesis be explained by the well-known fluctuating levels of estrin? Granted that the estrin stimulation was at one time sufficient to produce endometrial hyperplasia and fibroids, it does not necessarily follow that this level has to be maintained continually. Once the fibroids have been formed, their change to estrin fluctuations is minimal, while endometrial changes to the estrogenic hormonal level is much more sensitive and rapid. Possibly Dr. Kanter operated upon his patients at a time when half of them were at a low estrin phase.

And a last point which Dr. Kanter makes is, "Again, we must disagree with Witherspoon's contention that the sterility associated with fibromyomas is explained

totally by the hyperestrinism he believes is produced by the atretic follicles in the absence of corpora lutea." I firmly believe that on this point there must be a misinterpretation of my explanation for the associated sterility; my statement reads, "The explanation for the sterility in these three conditions (endometrial hyperplasia, fibroids, and endometriosis) is undoubtedly *lack of ovulation*, so well demonstrated in the ovaries by the presence of multiple follicle cysts and the absence of corpora lutea." I meant merely to infer by this statement that lack of ovulation (not hyperestrinism) was the cause of the associated sterility in women with fibroids, granted that mechanical factors (salpingitis, etc.) were excluded.

There are two experimental observations by Lacassagne relative to this subject that are of value: (1) "Progressive change in the uterus of rabbits submitted from birth to repeated injections of estrone" (Compt. rend. Soc. de biol. 120: 685-689, 1935), "Beginning on the third day of their birth six female rabbits were given weekly injections of folliculin benzoate, the amount being gradually increased from 1,000 international units to a maximum dose of 10,000 units after the lapse of two months. Five of the animals were sacrificed after 73, 99, 130, 169, and 851 days, respectively. It was found that the treatment had elicited a *fibromyomatous* transformation in the uterine wall and adenomatous proliferation in the cervix and the tubes. The findings strengthen notably the position of those clinicians who have long been referring endometrial hyperplasia, as well as uterine fibroids, to an excessive secretion of hormones." (2) "Progressive changes in the mouse uterus under the prolonged administration of estrone" (Idem 120: 1156-1158, 1935). "Weekly injections of 300 international units of estrone benzoate produced in the mouse uterus, after 11 to 584 days, changes resembling those already described in the rabbit."

J. THORNWELL WITHERSPOON, M.A. (OXON), M.D.

4008 N. Pennsylvania Street, Indianapolis, Ind.

REPLY BY DR. KANTER

Answering Dr. Witherspoon's letter of August 19, I have had the privilege of reading his letter previous to submission for publication. At that time I made the following comments to Dr. Witherspoon while urging him to publish his communication in order to stimulate interest in the subject.

We agree that the lack of endometriosis in colored women may be explained on the basis of the frequency of occurrence of salpingitis with closed tubes, but it fails of comprehension in explaining the similar rarity of internal endometriosis (adenomyosis) in this class of patient, this latter condition having no obvious relationship to closed fallopian tubes.

With regard to Dr. Witherspoon's explanation of the varying endometrial pictures found by us in our study, suffice it to say that such a question cannot be settled satisfactorily until such a time as a correlated study of blood estrin levels and endometrial histology is made upon a large series of patients.

Finally, Witherspoon contends lack of ovulation is the responsible factor in the production of sterility in patients with the fibroid, endometrial hyperplasia, endometriosis complex. The fact that we found corpora lutea in various stages of degeneration proves conclusively that these patients do ovulate.

Again, I feel that Dr. Witherspoon has done a great service in the field of research study. Such controversies are healthy and should serve to stimulate others to study these problems and possibly help us to settle the points that are in question.

AARON E. KANTER,

310 S. Michigan Ave., Chicago, Ill.

To the Editor:

In the August number of the JOURNAL in an article on "Triple Pregnancy Diagnosed by Means of X-ray," Margaret B. Ballard says, that a careful search of the available literature reveals only nine cases in which a diagnosis of triplets was made before delivery (Edling, Essen-Moeller, Favreau and Despons, Gennell, Johnston, Mareus, Rowden, Trillat, Eparvier and Naussac and Aldredge). She then briefly describes these nine cases and adds a case of her own. In Edling's case the correct diagnosis was made only after delivery.

For the sake of completeness, may I add two more cases. In 1923 I presented an illustration of the third case reported in the literature of triplets demonstrated on an x-ray plate. (The Value of X-ray in Obstetrics, *Medical Clinics of North America* 7: 611, 1934.) The two reports which preceded this article were those by Edling and by Essen-Moeller. My case was similar to that reported by Edling in one respect, namely, that the correct diagnosis was not made until the x-ray plates were reexamined after delivery. In Edling's case an x-ray picture taken at the fourth month resulted in a diagnosis of twins, but after delivery, evidences of the third baby were discovered on the x-ray plate. In the case I reported, a diagnosis of triplets or twins with polyhydramnios was made before delivery. An x-ray picture was taken but only two heads were seen. However, after delivery of the three babies, reexamination of the x-ray plate revealed the third head.

The second case I should like to add is that reported by Weil (*Grossesse Trigémellaire, Gynécologie et Obstétrique* 32: 289, 1935). In two additional cases of triplets reported by Weil the x-ray plates aroused a suspicion of triplets but three fetuses could not be definitely detected on the x-ray plates.

In the world literature there are four cases of quadruplets demonstrated by x-ray examination. The first was reported by Hermstein and Pfalz (*München. med. Wehnschr.* 78: 492, 1931). The second and third cases were reported by E. U. Williams (*Brit. M. J.* 2: 1206, 1935). The fourth case was reported by Dawson (*J. Obst. & Gynaec. Brit. Emp.* 43: 252, 1936).

J. P. GREENHILL, M.D.,
55 E. WASHINGTON STREET,
Chicago, Ill.

Umbilical Cord Clamp

To the Editor:

In my article describing an improved umbilical cord clamp, published in the September, 1936, issue of the JOURNAL, page 513, I failed to give credit to Dr. Charles E. Ziegler of Pittsburgh, Pa., who described a special device of this kind in a paper entitled "Additions to Our Obstetric Armamentarium," which appeared in the JOURNAL in January, 1922.

The latter was published two months prior to the paper by Willson, referred to by me and which was included in the March, 1922, issue of the same JOURNAL.

MILTON E. KAHN, M.D.
BUFFALO, N. Y.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Physiology of Labor

Robinson, Datnow, and Jeffcoate: *Induction of Abortion and Labour by Means of Oestrin*, Brit. M. J. 1: 749, 1935.

It is believed that during pregnancy expulsive contractions of the uterus are held in abeyance by a state of equilibrium in the hormones, progesterin and estrin. These hormones have been shown to have a contrary effect on the uterus, the former inhibiting, the latter stimulating, uterine activity. Induction of labor with estrin was accomplished in rodents but not in human beings.

Estrin is not directly oxytocic; it has no effect on the isolated uterus and only acts when given parenterally to the animal. It has a long latent period of activity, and produces its effect (1) by causing hypertrophy of the muscle fibers and hyperemia of the uterus, (2) by sensitizing the muscle and nerve elements of the uterus, and (3) by stimulating the production of infundibulin in the body.

A series of experiments in the human being is recorded, showing results obtained with the use of estrin during different stages of normal and abnormal pregnancy. The hormone was effective in stimulating uterine activity in cases of missed abortion, thus confirming the work of others who claim that the retention of the dead fetus is associated with an absence of estrin in the blood. Estrin is useful in primary uterine inertia.

F. L. ADAIR AND S. A. PEARL.

Knaus, H.: *The Causes of the Onset of Labor*, Med. Klin. 30: 1649, 1934.

In the opinion of Knaus the onset of labor is dependent upon two factors. The first is the uterine musculature. During pregnancy, the uterine muscle gradually increases its tonicity and power of contractility. When the corpus luteum degenerates, it releases its control on the uterine musculature so that the muscle may react to the hormone of the posterior pituitary lobe. This hormone is what initiates labor. As long as the corpus luteum is active the posterior pituitary secretion cannot act on the uterine muscle. This pituitary secretion is also influenced by the placenta, because it contains a substance (the anterior pituitary-like hormone) which has a luteinizing effect. Whereas the estrus hormone produced by the placenta increases with the duration of pregnancy, the pituitary-like hormone production in the placenta decreases with the advance in pregnancy. The result of this is that the corpus luteum gradually degenerates in the second half of pregnancy. As this occurs the highly contractile uterine musculature becomes more and more susceptible to the posterior pituitary secretion. At the end of pregnancy, the corpus luteum has absolutely no inhibitory effect on the uterine muscle, and the posterior pituitary hormone acts on the uterine musculature to initiate labor.

J. P. GREENHILL.

Voron and Contamin: Induction of Labor by the Combined Use of Folliculin and Pituitary Substance in Prolonged Pregnancy, *Bull. Soc. d'obst. et de gynéc.* 24: 68, 1935.

Because it is known that folliculin sensitizes the uterine musculature to the action of an oxytocic, the authors attempted to use both folliculin and posterior pituitary substance in three cases of prolonged pregnancy. In two cases they obtained contractions within a few hours after the injections were given. The contractions continued until the fetuses were expelled. The authors, therefore, recommend this procedure and consider it entirely harmless.

J. P. GREENHILL.

Bock, A.: pH Determinations of the Vaginal Secretions and of the Amniotic Fluid in an Attempt to Determine Rupture of the Membranes, *Arch. f. Gynäk.* 155: 443, 1934.

The author made pH determinations of the vaginal secretions and of the amniotic fluid of pregnant women in the attempt to discover a possible change after rupture of the membranes.

He found that the pH concentration of the vaginal secretion was 5.2 to 6.0 when the membranes were still intact. He ascertained values of 7.0 to 7.5 for the amniotic fluid. The values in the vaginal secretions in healthy women in labor and after the rupture of the membranes were 7.0 or higher. He, therefore, concludes that pH concentration of 6.0 or less is definite evidence that the membranes are intact.

RALPH A. REIS.

Coatz, Alberto S.: The Etiology of Premature Rupture of Membranes, *Obst. y ginec. (Buenos Aires)* 14: 529, 1935.

The author found the incidence of premature rupture of the membranes to be 8.3 per cent. In 81 per cent of cases the rupture of the membranes occurred at the end of labor. There is no relationship between the time of rupture of membranes and the constitution of the patient or the growth of the pregnancy. Of the cases studied, 60 per cent were multiparas.

Occupation, coitus, traumatism have no influence on premature rupture of membranes. Metritis and its consequences, abnormal adhesions and great thinness of the membranes could be causative agents.

The author believes that neither malposition of the presenting part nor false labor pains lead to premature rupture of membranes.

MARIO A. CASTALLO.

Winter, E. W.: The Premature and Very Early Rupture of the Membranes, *Monatschr. f. Geburtsh. u. Gynäk.* 99: 332, 1935.

At the Giessen Clinic among 573 women who had premature rupture of the membranes, 4 women died as the result of this complication. Likewise, 9 per cent of the viable children also perished as the result of the untimely rupture of the membranes. Hence, the author considers this complication to be a very serious one. It occurs in about 20 per cent of all cases. Many women developed puerperal infections. Intrauterine manipulation must be carried out more frequently and serious consequences may result from this. The longer the period of time which intervenes between rupture of the membranes and the onset of pains the worse the prognosis. Every woman who has premature rupture of the membranes should be delivered in a hospital.

J. P. GREENHILL.

Higgins, L. G.: Induction of Labour, Brit. M. J. 2: 721, 1935.

The author presents clinical data indicating favorable results from simple rupture of the bag of waters for induction of labor. These views are supported by observations made by Fitzgibbon, Morton, Berger and Stroganoff on normal, post-mature, and eclamptic patients, respectively.

The author believes this method of induction approximates closely to the normal onset of labor. It is suggested that there is no evidence that artificial rupture of the membranes under suitable conditions increases the tendency to pyrexia in the puerperium. Nor has any relation been established between pyrexia and the length of time which elapses between artificial rupture of membranes and the onset of labor. No prejudicial effect upon the child due to early rupture of the membranes has ever been ascertained.

F. L. ADAIR AND S. A. PEARL.

Blair, E. Murray: Induction of Labour by Rupture of the Membranes, Canad. M. A. J. 34: 49, 1936.

The author discusses inductions of labor in general and points out the failures with medical routines. He outlines the actions of the various factors before labor can be precipitated as: (1) The presence of estrin in sufficient quantity to (a) sensitize the uterine fibers and (b) call forth enough infundibulin to cause contractions; (2) the absence of progesterin, enough that the contractions be not inhibited; (3) enough infundibulin must be brought into the circulation by estrin to promote labor contractions.

It is pointed out that rupture of the membrane is a means of inducing labor; that "dry labor" is not the bugbear it was once considered; and that rupturing the membranes has a place in the treatment of eclampsia.

He concludes that rupture of membranes is the surest procedure in inducing labor at full term; its risks are not as great as they have been considered. However, he does not uphold rupture of the membranes as a routine method of induction.

H. CLOSE HESSELTINE.

Furtado, Affonso Henriques: Fetal Asphyxia Due to Artificial Rupture of the Membrane in a Case With Membranous Insertion of the Cord, Rev. de gynec. e d'obst. 29: 629, 1935.

This report concerns a multipara, aged thirty-seven, who had been in labor for four hours. She was progressing normally, the fetus in cephalic position, the fetal heartbeats 140 per minute. After complete dilatation of the cervix, the membranes were ruptured artificially. Ten minutes later the patient delivered an apparently dead baby which was, however, revived by artificial respiration. The placenta was delivered spontaneously forty minutes after the baby was born. On examination of the placenta it was found that the cord was attached to the membranes.

F. L. ADAIR AND J. SUAREZ.

Ganner, Philip J.: Results of Ante-Natal Administration of Quinine, Brit. M. J. 2: 205, 1935.

The use of quinine in the last weeks of pregnancy is revived. The idea is an old one, but the literature on the subject is scanty. Certain advantages are claimed for it by those who used it, and, therefore, it deserves further trial.

The author reports a series of 50 normal primiparas who received 2 gr. of quinine bichloride t.i.d., from the thirty-sixth week of pregnancy onward. The results

are tabulated, and he concludes that the tendency to onset of premature labor is diminished by the antenatal administration of quinine and that the first and second stages of labor are accelerated without damage to mother or child. Inertia is not entirely abolished. In his small series of cases, there were no retained placentas or severe postpartum hemorrhages. An increase of uterine activity possibly exists in the third stage also. There appears to be no evidence of any influence on involution and the puerperium.

In all, the uterine action is strengthened by giving small doses of quinine during the last month of pregnancy. Since good uterine contractions are a very valuable factor in obstetrics, this method becomes commendable, if the fact is finally established and accepted by the profession. A method which secures good uterine contractions and is simple and safe for use in domestic practice deserves thorough investigation and more attention than it has had up to the present time.

F. L. ADAIR AND S. A. PEARL.

Mitchell, D. A., and Bradbrooke, H. N.: Further Experience of the Use of Quinine in Normal Labor, *Brit. M. J.* 2: 206, 1935.

In 1930, the author had published material on the use of quinine antepartum in a series of 400 cases. He adds enthusiastically to its merits in the present study. Claim is made that the general health of the patients is improved due to the tonic action of quinine in small doses. Often dyspepsia and heartburn in the later weeks of pregnancy are corrected by it. Labor is made easier and shorter. The first stage of labor proceeds almost imperceptibly and painlessly to the patient. The second stage is more forceful and shortened. Uterine retraction is uniformly good. Clots were rarely seen forty-eight hours following labor in the series of quinized patients. There is no increased tendency to premature or precipitate labor. Retained placenta is uncommon; in fact, cases with a history of such and postpartum hemorrhage in previous labor were treated successfully with quinine prenatally. Perineal lacerations and afterpains are not increased by its use. In the abnormal cases each one must be considered on its own merits. The drug is of greatest aid in normal labor; it is contraindicated in any condition in which slow labor is desirable for the purpose of molding.

The author emphasizes the administration of the drug in small repeated doses. Attempts to use larger doses will only bring the method into disrepute. Quinine has not been proved to be an initiator of uterine contractions. It acts as a tonic, increasing the basic tone of the uterine muscles, and reinforces contractions which are excited by endogenous means. This tonic action is produced by a small dose; larger doses may cause inertia or paralysis of uterine muscles. The dose should not exceed $1\frac{1}{2}$ to 2 gr. t.i.d. for two to three weeks before labor is expected. A single daily large dose is contraindicated.

F. L. ADAIR AND S. A. PEARL.

Goecke, H.: The Significance of the Number of Pains in Cases of Premature Rupture of the Membranes Especially in Primiparas With Normal Pelves, *Monatsschr. f. Geburtsh. u. Gynäk.* 99: 24, 1935.

During the past few years Frey has written many articles attempting to prove that a knowledge of the actual number of labor pains is of the utmost significance in the conduct of labor. Frey claims that if labor does not terminate spontaneously after a specific number of labor pains, depending upon the parity and intactness of the membranes, interference will become necessary. Goecke studied a large series of cases but could not substantiate Frey's contention. He found that patients did deliver spontaneously after they had passed the so-called maximum number of

uterine contractions. He therefore warns against terminating labor by artificial means simply because a patient has had a certain number of labor pains. This warning is particularly important in cases where Frey's maximum number of pains is exceeded before there is complete dilatation of the cervix and where therefore a cesarean section or other operation would be advocated by him.

J. P. GREENHILL.

Defendi, S.: The Number of Uterine Contractions During the Various Phases of Labor, *Folia Gynaec.-demog.* 32: 529, 1935.

The author states that the results obtained from the counting of the uterine contractions during the labor of 110 primiparas and 100 multiparas, done according to the theory of Frey, demonstrate such a variability of values that these do not permit acceptable deductions in regard to prognosis or necessary interference.

MARIO A. CASTALLO.

Consoli, D.: The Action of the Lower Uterine Segment During Labor, *Clin. Ostet.* 37: 385, 1935.

After briefly describing the anatomy and histology of the uterus, the author discusses the action of the lower uterine segment during labor. He concludes that during labor two phases can be distinguished in the lower uterine segment:

1. A passive one designated by the contractions of the two internal layers of the uterus with a minimal participation of the external longitudinal layer, which only serves at this period to support and coordinate with the functions of the other layers. The lower uterine segment at this time is simply stretched, having no sign of contractions in its fibers. Such passive distention, due to the descent of the ovum, reduces the tonicity of the fibers of the uterine os and produces dilatation.

2. The other phase is active and is designated by the contractions of the external layer. The transmission of the contractions of the longitudinal fibers of the body to the lower segment causes a shortening of the cervical margins, giving rise to the real progress of dilatation, which finally leads to the termination of labor.

AUGUST F. DARO.

Sciclounoff, T.: Inquiry Into the Value of Rectal Examinations During Labor, *Rev. franç. de gynéc. et d'obstet.* 30: 1, 1935.

The author sent out 280 questionnaires concerning the value of rectal examinations. He received 115 answers, and from an analysis of these replies he comes to the following conclusions: Rectal examinations alone are used by only 7.9 per cent of obstetricians. It is considered by 72 per cent to be insufficient for all normal and abnormal cases. However, 21 per cent of obstetricians believe that rectal examinations suffice for normal cases but not for the abnormal ones. The majority of obstetricians believe that vaginal examinations are indispensable for midwives. The majority of heads of departments permit vaginal examinations to be made by students. Three-fourths of all the obstetricians who answered consider vaginal examinations harmless when practiced according to a rigid technic. The author himself maintains that labor may be conducted in the large majority of cases by external examinations alone. When necessary, vaginal examinations should supplement abdominal examinations. He is opposed to rectal examinations because they are much more difficult to make than vaginal examinations, and it is difficult to teach students by this method.

J. P. GREENHILL.

Farkas, J.: The Question of the Movable Head in Primiparas, *Monatschr. f. Geburtsh. u. Gynäk.* 100: 138, 1935.

In the Budapest Midwife School, Farkas found that among 3,829 primiparas, the head was floating at the inlet in 305 cases, an incidence of 8 per cent. The pelvis was contracted in only 50 of these women, hence the head was movable in 6.7 per cent of all primiparas with normal pelvis. In 87.3 per cent of these women, delivery occurred spontaneously; therefore a movable head in a primipara is not necessarily a pathologic condition. In fact, in 15 per cent of the cases, labor was completed within a very short time. In the author's opinion the chief cause for the delay in the engagement of the head lies in the increased resistance of the lower uterine segment and not in the condition of the abdominal wall or the uterine contractions. The author advises that primiparas in whom the head is not engaged at the onset of labor should be delivered in a hospital.

J. P. GREENHILL.

Items

American Board of Obstetrics and Gynecology

The next written examination and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology will be held in various cities in the United States and Canada on Saturday, March 6, 1937.

The next general examination for all candidates (Groups A and B) will be held in Atlantic City, N. J., on June 8 and 9, 1937, immediately prior to the American Medical Association meeting.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for these examinations must be filed in the Secretary's office not later than sixty days prior to the scheduled date of examination.

The American Board of Internal Medicine (Inc.)

The American Board of Internal Medicine, incorporated February 28, 1936, completed its organization on June 15, 1936. The officers chosen were Walter L. Bierring, M.D., Des Moines, Chairman; Jonathan C. Meakins, M.D., Montreal, Vice-Chairman; and O. H. Perry Pepper, M.D., Philadelphia, Secretary-Treasurer. These officers with the following six members constitute the present membership of the Board: David P. Barr, M.D., St. Louis; Reginald Fitz, M.D., Boston; Ernest E. Irons, M.D., Chicago; William S. Middleton, M.D., Madison; John H. Musser, M.D., New Orleans, and G. Gill Richards, M.D., Salt Lake City.

The term of office of each member will be three years, and no member can serve more than two consecutive three-year terms.

The organization of the Board is the result of effective effort on the part of the American College of Physicians in conjunction with the Section on Practice of Medicine of the American Medical Association and these two organizations are represented in the membership of the Board on a five to four ratio, respectively.

The American Board of Internal Medicine had previously received the official approval of the two bodies fostering its organization, as well as that of the Advisory Board for Medical Specialties and the Council on Medical Education and Hospitals of the American Medical Association.

The purpose of the Board will be the certification of specialists in the field of internal medicine, and the establishment of qualifications with the required examination procedure for such certification.

While the Board is at present chiefly concerned with the qualification and procedure for certification in the general field of internal medicine, it is intended to inaugurate immediately after July 1, 1937, similar qualification and procedure for additional certification in certain of the more restricted and specialized branches of internal medicine, as gastroenterology, cardiology, metabolic diseases, tuberculosis, allergic diseases, et cetera. Such special certification will be considered only for candidates who have passed at least the written examination required for certification in general internal medicine. The operation of such a plan will require the active participation and cooperation of recognized representatives from each of such special fields of medicine.

The first written examination will be held in December, 1936, and candidates successful in this written test will be eligible for the first practical or clinical examination which will be conducted by members of the Board near the time for the annual session of the American College of Physicians at St. Louis in April, 1937. The second practical examination will be held at Philadelphia near the time of the annual session of the American Medical Association in Atlantic City in June, 1937.

Application blanks and further information can be obtained by addressing the office of the chairman, Walter L. Biering, M.D., 406 Sixth Avenue, Des Moines, Iowa, U. S. A.

Books Received

CONTRACEPTION AS A THERAPEUTIC MEASURE. By Bessie L. Moses, M.D. 90 pages. The Williams & Wilkins Company, Baltimore, 1936.

MEDICAL HISTORY OF CONTRACEPTION. By Norman E. Hines, Ph.D. Illustrated, 521 pages. The Williams & Wilkins Company, Baltimore, 1936.

A MANUAL OF PRACTICAL OBSTETRICS. By O'Donel Brown, assistant gynecologist, Sir Patrick Dun's Hospital, Dublin, etc. With 10 plates, some in color, and 236 illustrations, 363 pages. William Woods & Company, Baltimore, 1936.

SYPHILIS AND ITS TREATMENT. By William A. Hinton, M.D., Boston, Mass. 321 pages. The Macmillan Company, New York, 1936.

GYNECOLOGY FOR NURSES. By Harry Sturgeon Crossen, Professor Emeritus of Clinical Gynecology, Washington University School of Medicine, etc., and Robert James Crossen, Instructor in Clinical Gynecology and Obstetrics, Washington University School of Medicine, etc. Second edition, with 356 engravings including one color plate. 316 pages. The C. V. Mosby Company, St. Louis, 1936.

POST-GRADUATE SURGERY. Edited by Rodney Maingot, Senior Surgeon to the Royal Waterloo Hospital and to the Southend General Hospital, etc. Volume II. With 1134 figures in the text, 3572 pages. D. Appleton-Century Company, New York, 1936.

THE PATIENT AND THE WEATHER. By William F. Peterson, M.D. Volume I, Part 2. Autonomic Integration. Illustrated, 781 pages. Edwards Brothers, Inc., Ann Arbor, Mich., 1936.

American Journal of Obstetrics and Gynecology

VOL. 32

DECEMBER, 1936

No. 6

Original Communications

PYELITIS IN TOXEMIAS OF PREGNANCY

JOHN P. PETERS, M.D., PAUL H. LAVIETES, M.D., AND
HARRY M. ZIMMERMAN, M.D., NEW HAVEN, CONN.

*(From the Departments of Internal Medicine and of Pathology, Yale University
School of Medicine.)*

IT IS becoming increasingly apparent that the term "toxemia of pregnancy" has little but tradition to recommend it and that the assumption which it implies is unjustifiable. No etiologic toxic products have yet been found by the most ardent advocates of the toxemia theory. There is increasing recognition of the fact that the syndromes encountered in the toxemias differ only in their incidence and speed of development from similar pathologic conditions that occur in non-pregnant women and in males. The question naturally arises whether the fundamental etiologic factors may not also be identical and whether pregnancy does not act only as the predisposing or precipitating cause for an acute explosion. One means of testing this theory is to analyze cases in which recognized renal or vascular diseases occur in conjunction with pregnancy. The most obvious condition of this kind is pyelitis.

MATERIAL AND RESULTS

For the purpose of this investigation, first of all, the records of all cases that received a diagnosis of toxemia of pregnancy in the New Haven Hospital from 1922 to 1935 inclusive, were collected and reviewed. To these were added 11 patients from the medical service of the hospital who had renal or vascular diseases that began during pregnancy. Finally the records were searched for patients with pyelitis during pregnancy who did not develop toxemia or receive the diagnosis "toxemia." Altogether there were between 350 and 400 cases in the first two

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

groups, of which only 320 were accepted. The others were rejected either because their records were entirely inadequate or because they did not have toxemias of the type under consideration, but only severe vomiting of early pregnancy. The accepted cases are of uneven value because diagnostic procedures, therapy, and subsequent observations were not uniformly controlled by any one person with a specific purpose. A large number, however, were seen by the senior author or members of his staff, and many were followed for variable periods in the metabolism clinic.

✓ Of the 320 cases, 41, or 13 per cent, suffered at one time or another from conditions generally included under the terms pyelitis or pyelonephritis. There is sufficient evidence in many other cases to indicate that the actual incidence of the condition was far greater; but only those cases about which there could be no uncertainty are included in this group. Abstracts of the protocols are presented at the end of the paper.

Among the 41 cases 11 came to autopsy, where the condition was verified. The first 12 protocols give the records of these cases, and of one other, A 32,601, who is added for reasons mentioned below. This represents 44 per cent of the 25 known toxemia patients on whom autopsies were made during the period covered by this report, strengthening the impression that the condition occurs more frequently than it is recognized. These autopsied cases provide a sounder basis for analysis than the others and will, therefore, be discussed first.

The first case, A 39,242, presented an extremely acute picture which seemed to originate during pregnancy and culminated in a rapidly fatal eclamptic syndrome during delivery. At autopsy acute bilateral pyelonephritis was discovered. Case 2, A 1,714, had toxemias in two successive pregnancies, the second typically eclamptic and fatal. Besides an acute bilateral pyelitis and ureteritis, she had a hydronephrosis with secondary changes in the kidney that can have been the result only of a longer-standing condition that may well have originated from her previous pregnancy toxemia. Case 3 (3,666) after two toxemias developed a fatal suppurative pyelitis and cystitis. At autopsy, besides the acute infection, a chronic hydronephrosis was found with secondary changes which indicated a disease of longer duration than that of the first two cases. Case 4 (63,494) beginning with an acute eclamptic seizure at the end of her first pregnancy, associated with pyuria, subsequently ran the usual course of chronic infected bilateral hydronephrosis, terminating fatally five years later. At autopsy extreme secondarily contracted pyelonephritic kidneys were discovered, together with the characteristic lesions in the general vasculature. Case 5 (44,154) is quite similar except that the disease ran a far longer course, altogether twenty-two years. It is quite probable that the abdominal pains of which she complained for so many of these years were all referable to the renal condition. Case 6 (A 9,526) had a comparable history, but was not seen during the original pyelitis. The same is true of Case 7 (8,250) moreover, in this case a congenital anomaly of the urinary tract may have played a contributory rôle. In Case 8 (31,841) pyelitis developed out of pregnancy, which seems merely to have aggravated the condition. A congenital anomaly which caused obstruction of the lower urinary tract undoubtedly acted as a predisposing cause for the pathologic lesions found in Case 9 (47,162) who had a typical eclamptic toxemia. Case 10 (29,869) is included in the autopsy category; however, the autopsy was performed at another hospital, where she died, and contributes little because the report is so inadequate. In Case 11 (53,431) the patient died from adventitious causes five years after the initial toxemia, had no pyelitis or pyelonephritis at autopsy, but did exhibit signs of permanent injury from previous disease in dilatation of the right renal pelvis and ureter. Case 12 (A 32,601) has not been included in the roll of pyelitic subjects. The immediate cause of her death was bronchopneumonia. In addition she had pathologic lesions in liver and kidney which

are usually connected with eclampsia. The dilatation of the right ureter and renal pelvis, unaccompanied by infection of the urinary tract, are probably only part of the changes found in normal pregnancy.

The next seven patients died, but did not come to autopsy. Among these pyelitis or hydronephrosis, or both, were demonstrated by cystoscopic examination at some time in four, Cases 13, 16, 17 and 18 (37,453, 20,921, 55,527, and 15,177). In the others the diagnoses were made from symptoms and urinary findings only. In four, Cases 16, 17, 18 and 19 (20,921, 55,527, 15,177, 23,706) death occurred long after the original pyelitis, which seems to have originated during a toxemic pregnancy in 15,177 and 23,706 and in the other two to have preceded the pregnancies in which toxemias appeared. These cases resemble in all respects those of the autopsy series who had secondarily contracted pyelitic kidneys. One of those who had pyelitis preceding her toxemic pregnancy, Case 17 (55,527) had a typical eclamptic syndrome. The remaining three, Cases 13, 14, 15 (37,453, 35,348 and A 9,052) died of fulminating toxemias. The first had eclampsia; the second died three weeks after delivery; the course of the third resembled closely that of Case 2 (A 1,714) of the autopsy series. Only Case 13 (37,453) is known to have had pyelitis before the onset of her toxemic pregnancy, and this originated in an earlier pregnancy that was terminated.

The remaining 23 comprise an extremely miscellaneous group of cases. The diagnosis in 13, Cases 20 to 32 (53,658 to 26,573 inclusive) was established by means of the cystoscope or intravenous pyelography, in the remainder by symptoms, signs, and urinary findings. There are three instances of eclampsia: one in Case 20 (53,658) with pyelitis which arose during pregnancy and, in spite of treatment before and after delivery, left permanent and irreparable marks in the urinary tract; one in Case 41 (81,771) who, twenty-five years later, had the hypertension and associated signs of vascular disease that mark the advanced stages of chronic contracted hydronephrotic kidneys; the third in Case 33 (70,951) who had an unmistakable pyelitis although the diagnosis was not established by cystoscope or pyelograms. The fate of this patient is not known. The other 12 who had cystoscopies exhibited toxemias of every variety and of every degree of severity. In fact some of the syndromes were so mild as hardly to deserve the appellation of toxemia.

Of the remaining cases, in which the diagnosis was not established by direct examination of the urinary tract, but little need be said. These examinations were not made, usually because the urinary infection was relatively slight or because the period of observation was short. It is natural to find in this group the least severe cases. Nevertheless, the ultimate severity cannot be predicted from the character of the symptoms in the initial stages of the disease, as the records of some of the cases in the earlier groups testify.

DISCUSSION

It has now been established that in the majority of normal women in the latter part of pregnancy, the pelves of the kidneys and the ureters above the pelvic brim are dilated, owing to some obstruction of the intrapelvic portions of the ureters.¹⁻⁹ Whether this condition results from compression by the gravid uterus or from hyperplastic changes in the pelvic portions of the ureters is of little importance for the present argument. The right ureter is more frequently and more seriously affected. It has been clearly recognized that this condition subjects the pregnant woman to greater risk from pyelitis,^{2, 10-16} increases the dangers of pyelitis and militates against its effective treatment. The tendency for pyelitis to become chronic and to recur in

future pregnancies has been noted by Kretschmer,¹⁵ Crabtree and Prather¹⁶ and others. The relation of these anatomical distortions and infections of the urinary tract to toxemias has, however, received little emphasis, or else it has been too generally assumed that these toxemias differ from those which are not accompanied by pyelitis or pyelonephritis.

Willenweber¹⁸ made the suggestion that pressure in the renal pelvis during pregnancy, by impairing kidney function, gave rise to the toxemias. This hypothesis can hardly be accepted in view of the now recognized frequency of hydronephrosis and increased ureteral pressure. Some additional factor must be hypothesized. Williams¹³ and Hunner¹⁴ in calling attention to the seriousness of pyelitis in pregnancy cite each one case that developed symptoms or signs of toxemia, but the significance of these in relation to the pyelitis either escaped attention or was not especially emphasized. In most of the other reports cited above attention was confined to urologic aspects of the disease to the exclusion of general systemic manifestations or functional disturbances. Rockwood, Mussey and Keith,¹⁹ after reviewing 100 consecutive cases of toxemia, concluded that they conformed in general with renal and vascular diseases encountered in nonpregnant subjects, according to the classification of Volhard and Fahr. In this classification pyelitis and pyelonephritis form one category to which Rockwood, Mussey and Keith consigned 34 out of the 100 cases. None of these is described in the report, but under the heading of acute nephritis appears a patient whose history is marked by pains in the back and abdomen and pyuria who proved at death, after recurrent toxemias, to have bilateral infected hydronephrosis. Because this subject presented initially edema, hypertension, and other signs of toxemia, the pyelonephritis is looked upon as a complication of an acute nephritis. Kahn,²⁰ largely on the basis of bacteriologic studies of the urine, with more extensive examination in certain cases, found some evidences of pyelitis in 40 out of 52 cases of toxemia which he examined. Hirst²¹ suggested that there was some relation between anatomic obstruction and infection of the urinary tract and the late toxemias of pregnancy. O'Sullivan²² in a discussion of "albuminuria in pregnancy" recognizes two major classes, those without and those with bacilluria. Of 67 cases, 46 belonged to the latter group and of these 10 had hypertension. He calls attention to the fact that pain, dysuria, and other symptoms of urinary tract infection may be absent, and blood chemistry and functional tests may be normal in these cases. Edema was frequent. The course was often afebrile until the puerperium; but after delivery fever was the rule, whereas it was rare in patients without bacilluria. In both classes respiratory infections frequently preceded the onset of toxemia. Evans,²³ in a follow-up study found that 4 out of 76 patients with noneclamptic toxemias, after intervals of from four months to four years had definite cystitis or pyelitis. McIlwraith²⁴ recognizes infective nephritis with positive urine cultures as one of the causes of eclamptic or preeclamptic toxemias. Bell,²⁵ in 10 autopsies of patients who died from eclampsia, found the right ureter dilated 3 times, the bladder twice, and the left ureter once. This, in itself, means little. Since some degree of hydronephrosis is so commonly a part of pregnancy, it is only surprising that he did not find it more often.

This does not pretend to be an exhaustive review of the voluminous literature on the urinary disorders of pregnancy, but is believed to be fairly representative of opinions on the subject, especially in relation to toxemias. Throughout there is a striking tendency to separate pyelitis of pregnancy from other toxemias, apparently chiefly because

it has a more definite pathogenesis. This exhibits itself in a general tolerance to more conservative treatment, which is strangely (inconsonant) with the repeated confession that pyelitis, even without toxemic complications, if it extends into the latter months of pregnancy, when ureteral obstruction is established, is extremely refractory to treatment, can seldom be cured before delivery, leaves permanent anatomical residua, and is likely to recur in a more aggravated form in subsequent pregnancies.

In relation to the course of disease the cases here reported can be divided into four classes: (1) Those who developed pyelitis before the particular pregnancy in which toxemia occurred; (2) those who developed pyelitis early in pregnancy; (3) those in whom pyelitis was discovered during the puerperium; (4) a small number who had antecedent toxemias and later developed, or were found to have, pyelitis. The relation to toxemias of the pyelitis and pyelonephritis in the last two classes is especially open to question. In many, if not most, of the cases in which pyelitis was not discovered until the puerperium, it is not improbable that it had preceded labor without having been recognized. This was evidently the order of events in Cases 3 and 2 (3,666 and A 1,714), as the postmortem findings testify. In the latter there is good reason to believe that hydronephrosis attended a preceding toxemic pregnancy in which no symptoms of pyelitis were recognized. It is not possible to secure equally good evidence in the cases of Class 4 who did not come to autopsy.

Of the 41 patients, 25 had outspoken toxemias, 9 with eclamptic seizures. Four had hypertension or edema or both. One had pregnancy terminated early. The remaining 11 either were not seen in their initial illnesses or else were delivered elsewhere. In these the diagnosis of toxemia depends on anamnesis or the subsequent clinical course. Almost all received a diagnosis of toxemia of one kind or another. To maintain that in the most authentic cases the coexistence of pyelitis and toxemia was only coincidental would be less than open-minded so long as the true cause and nature of toxemias are still unknown.

It is relevant to inquire why, if toxemias so commonly result from pyelitis, the fact has not long since commanded more recognition from urologists as well as obstetricians. It seemed profitable, therefore, to search the records of the hospital for cases of pyelitis occurring in the course of pregnancy in which the diagnosis of toxemia was not made. It was found that out of 93 such cases, 25 developed before term definite hypertension (systolic pressure 150 or over; diastolic 90 or over), sometimes accompanied by edema. The number would probably have been larger if more assiduous attention had been given to examination of blood pressure. Considering that the records examined include subjects who had pyelitis which subsided in the early months of preg-

nancy, and others who could not be observed throughout pregnancy, the proportion who developed signs suggesting toxemia is by no means insignificant. If these 25 patients are included among the pyelitic toxemias the number of these is swelled to 66, or 19 per cent of all the toxemias. In addition to those who developed hypertension and edema, there is a large group of patients who, after pyelitis of pregnancy proved to have permanent anatomical injuries of the urinary tract, hydronephrosis, ureteral strictures, etc.

If a relation between pyelitis and toxemias is admitted, current concepts concerning the etiology and pathogenesis of the latter are hardly tenable. Nine of the patients in this series had typical attacks of eclampsia. In many of these the existence of pyelitis had been established in advance of the toxemia, in some it had long preceded the toxemia. In this connection the patient, Case 9 (47,162) in the autopsy group, is particularly illuminating because she had a congenital lesion of the urinary tract which had evidenced itself in hyposthenuria and albuminuria long before her first pregnancy. Instead of eclampsia, then, she should have presented the pictures which are described under the terms, "low reserve kidney" or "nephritis of pregnancy." To claim that the seizures which these patients had were not truly eclamptic implies a preconception about the nature of this type of toxemia for which there is no warrant. After all, the only features by which it can be distinguished are its sudden onset and the convulsive explosions, which are beautifully illustrated in such cases as 1, 13, 20, and 33 (A 39,242, 37,453, 53,658, and 70,951). Too much emphasis must not, however, be placed upon the association between pyelitis and eclampsia. Almost every clinical syndrome described among toxemias is illustrated by one or other of the cases which have been described. This is not surprising if it is appreciated that quite similar incidents may occur in the course of chronic pyelitis, hydronephrosis, and pyelonephritis without pregnancy. For example, in this series Cases 16, 17, and 8 (20,921, 55,527 and 31,841) had convulsive seizures subsequent to their toxemias, while the patients were neither pregnant nor in the terminal stages of their disease. This lends support to the earlier suggestion that the rôle of pregnancy in the etiology of toxemias may be merely to accelerate or exaggerate the progress of a pathologic condition which is of itself capable of producing a similar picture in the nonpregnant subject, evoking an acute explosion or exacerbation of the disease.

To deny the toxemic character of these cases entirely becomes an idle gesture in view of the fact that the great majority initially received the diagnosis of toxemia. Nor can this be ascribed to any peculiar local ignorance or negligence, since the records show that in many instances the original diagnosis of toxemia was made elsewhere, while the true condition was discovered here. The term toxemia may ill fit patients with pyelitis and pyelonephritis of pregnancy, but

it cannot be denied them without a redefinition of toxemia so radical that it would demand a complete revolution in the philosophic attitude toward these interesting complications of pregnancy, and would probably end in abolishing the term toxemia and all that it implies. However beneficial such a revision might be for the future, it cannot serve as a basis for retroactive criticism. The term "toxemia" has been applied broadly to certain symptoms occurring singly or in more or less characteristic complexes in the course of pregnancy, the chief of which are albuminuria, hypertension, edema, and convulsive seizures. These cases of pyelitis without exception exhibited one and usually more of these symptoms.

The postmortem pathology of the autopsied cases has not been described or discussed in detail, partly for lack of space, chiefly because this aspect of the subject will be discussed in a separate communication, dealing with the pathology of toxemias of pregnancy as a whole. To those who look upon morbid anatomy as the ultimate criterion for the differentiation of toxemias, it may be said that the patients who died in the acute stages of the disease presented, in addition to pyelonephritis, the tubular and glomerular changes which are considered characteristic of eclampsia, and in addition sometimes hemorrhagic and necrotic lesions of the liver. Lest it be claimed that these cases were probably exceptional instances in which pyelonephritis and eclampsia occurred coincidentally, we hasten to add that in the subsequent discussion of the pathology of toxemias, we hope to demonstrate that these lesions are characteristic of no particular type of toxemia and bear no clear relation to the details of the clinical syndrome nor to any antecedent pathologic condition which may have acted as a predisposing cause.

The failure to recognize the rôle of pyelitis earlier with more frequency may be attributed to the fact that it does not always manifest itself by the traditional signs and symptoms. Pain and lower urinary irritation may be almost or entirely lacking, although they appeared in this series more often than their significance was recognized. Experience gives the impression that they are especially likely to be inconspicuous in persons who have obstructive lesions of the urinary tract. This is exemplified by the autopsied Case 9 (47,162), and by other patients with congenital obstructive lesions in our own case records and in the recent reports of Longcope²⁶ and Ellis.²⁷ Just such an obstructive condition is provided by the well-recognized hydronephrosis of pregnancy, whether this be ascribed to pressure by the pregnant uterus or to morphologic changes in the walls of the ureters. Something more than the usual perfunctory prenatal examinations of urine and blood pressure is essential, if pyelitis is not to be overlooked. At the very least microscopic examination of a clean voided specimen as well as the routine test for albumin is indicated. Albuminuria, except in the most acute phases, may be inconspicuous, and

blood pressure may not rise until the toxemic explosion. More weight must be given to complaints of pain in the abdomen or back, urinary frequency and burning, and other subjective complaints that are too lightly attributed to irritability arising from the natural discomforts of pregnancy.

The seriousness of the association of pyelitis and pregnancy, if these protocols are typical, little justifies the casual attitude which it is usually accorded. The present series of cases represents a formidable group and includes subjects who received all the benefits of the most modern methods of treatment, although this phase of the subject has not been stressed in this report. It has long been clearly recognized that elimination of urinary infection in the presence of obstruction of the urinary tract is difficult, if not impossible. There is no reason to believe that in this respect a physiologic obstruction is more benign than a pathologic one.

Of the 41 cases presented, 7 died in the acute stages of toxemias; 10 after long and miserable illnesses, with secondarily contracted pyelitic kidneys. One, who died of adventitious causes, proved to have chronic hydronephrosis. Another 7, unless they have succumbed, are living with residua of the disease which will inevitably bring them to the same end. Six, after intervals of one to eight years, have symptoms or signs that suggest that they belong in the same class. Nine have been followed for such short periods or disappeared so early that it is impossible to predict their fate. On the basis of past experience it may be reasonably expected that a certain proportion of them will return to spend their last days of misery in the hands of the medical service. Only Case 24 (81,853) seems with any certainty to have escaped serious consequences; her pregnancy was terminated quite early, before any toxemic symptoms had developed, on the basis of the pyelitis alone.

One of the outstanding characteristics of pyelonephritis is its insidious progress and long duration. The duration of life after pyelitis became established in those of this series in which it can be accurately established was: Cases 4 (63,494), five years; 5 (44,154), twenty-three years; 6 (A 9,526), nineteen years; 7 (8,250), seventeen years; 8 (31,841), sixteen years; 9 (47,162), thirteen years; 16 (20,921), twelve years; 17 (55,527), seven years; 18 (15,177), six years; 19 (23,706), eighteen years; 30 (7,841), more than ten years, at least; 31 (34,922), over twenty-five years; 32 (26,573), over twelve years; 37 (35,865), at least four years; 41 (81,771), over twenty-five years. In contrast the term of happiness and health is pitifully short. Death usually comes after a long and lingering illness in which hypertension and its sequelae are much more in evidence than renal insufficiency. In fact it is notorious that a large proportion of these cases are mistaken for benign or malignant nephrosclerosis. The onset of hypertension is capricious in the extreme and for long periods the blood pressure may be so variable as to give the impression of a functional vasomotor disturbance. The urine much of the time seems relatively innocent, containing little or no albumin and only occasional white blood cells.

The course of the disease is, however, usually punctuated by recurrences or reerudescences of infection in which pyuria appears and hypertension and its associated evils advance.

Such advances are usually determined by the intervention of another pregnancy, in which toxemic symptoms frequently recur. Subsequent toxemias occurred in at least 10, probably 13, of the reported cases, a large proportion in view of the number who died of acute toxemias, those who had no subsequent pregnancies, those who were lost to view and those who have not yet had time to become pregnant again. In two cases the recurrences were frankly eclamptic, in both instances in patients who had originally eclampsia. It is frequently stated in the histories that subsequent pregnancies were uncomplicated. Such statements cannot be taken at their face value in view of the fact that, when objective examinations are available in similar cases, signs of toxemia are frequently observed. Nevertheless in individual pregnancies certain persons appear to escape unscathed. The factors which determine recurrence of toxemia remain to be discovered. There are vague suggestions in some of the protocols that the secondary disasters depend upon reinfection. The usual criteria of recovery, restoration of normal blood pressure and elimination of pyuria and albuminuria appear to be quite inadequate. Normal urine and blood pressure have been demonstrated in patients who have demonstrable hydro-nephrosis and in subjects in the advanced stage of the disease. Even renal functional tests fail to reveal the nature of the disorder until it has reached an advanced stage. Certainly the restoration of normal blood pressure and urine gives no insurance against a recurrence with subsequent pregnancies.

In the one patient who appears with reasonable certainty to have escaped sequelae or residua (Case 24, 81,853), pregnancy was terminated early for pyelitis alone, before toxemic symptoms had developed. Similar treatment in the other cases might not only have prevented untold suffering and untimely deaths; it might also, by enabling these women to rid themselves of their infections, have contributed ultimately more and better offspring. As is the case in all toxemias, the rôle of viable healthy children in behalf of which these pregnancies were allowed to continue is distressingly small. It is not only imperative that pyelitis of pregnancy be earlier and more frequently recognized, but that it be considered an indication for the termination of pregnancy. With the physiologic obstruction removed, continuous natural drainage is more likely to effect a cure than temporary or intermittent drainage secured by posture or instrumentation. And there may be hope that if the primary disease is cured it will not recur in subsequent pregnancies.

It is not intended to give the impression that pyelitis is or even may be the direct or remote cause of all pregnancy toxemias. It is believed that the present report underestimates its actual importance in the

production of these conditions. It is presumably, however, only one of a group of renal and vascular disorders which may serve this purpose. The reasons for this view will be presented in subsequent communications. Pyelitis has been selected for first consideration, because it is the most obvious of these disorders and can be demonstrated in the most unequivocal objective manner.

SUMMARY

Of 320 patients with toxemias of pregnancy, 41 were found to have pyelitis.

Of 25 autopsied patients with vascular or renal disease that first manifested itself in pregnancy, 11 were found to have pyelitis and hydronephrosis or their sequelae.

Of 93 patients with pyelitis complicating pregnancy, 25 developed, before pregnancy was terminated, hypertension or edema or both.

Reasons are given for believing that pyelitis in these patients was a major etiologic factor in the production of toxemia.

INDIVIDUAL CASE RECORDS

CASE 1.—Primipara, born 1911, entered hospital at term, Apr. 24, 1934. Extreme frequency and occasional pain after micturition, since onset of pregnancy; occasional dizzy spells and increasing edema for one month. B. P. 174/104, edema up to the knees. Insertion Voorhees' bag 7:30 P.M.; several convulsions beginning at 8 P.M. Death from circulatory and respiratory failure at 9 P.M. just after delivery of dead child by version and extraction.

Autopsy: Bilateral hydroureters and hydronephrosis; acute bilateral pyelitis; polynuclear infiltration of kidneys, especially near the pelvis; extensive necrosis of renal tubules.

CASE 2.—Born 1907. 1929, delivery at home after 7 weeks in bed with edema and hypertension. About June 1, 1931, in last month of pregnancy, edema of feet, extreme urinary frequency and burning. June 11, abdominal pain, followed by vomiting and later convulsions. Admitted to hospital comatose, with stertorous breathing, moderate edema of extremities, enlarged liver, jaundice, B. P. 182/130. Blood pressure fell rapidly, shock developed, with death in a few hours, temperature rising to 102.2°. Catheterized urine grossly bloody, with much albumin and many casts. N.P.N. 41.

Autopsy: Bilateral hydroureters and hydronephrosis with pyelitis, necrosis of renal tubules, acute hemorrhagic hepatitis. Hydronephrosis evidently of long standing, antedating immediate illness.

CASE 3.—Born 1898. Normal delivery 1917; delivery at 8 months for toxemia in 1919 with postpartum fever ascribed to puerperal infection; miscarriage at 5 months in July, 1921, after development of edema. After this exacerbation of long-standing "indigestion" (abdominal pain). About Nov. 1 sudden chill, acute dyspnea and orthopnea and severe headache, followed next day by persistent vomiting, muscular cramps, precordial and lumbar pain. (Illness was preceded by "cold in chest" with cough.) Later developed epistaxes, dizziness and blurred vision. Entered hospital Nov. 22, B. P. 170/120, retinal edema and hemorrhages, râles and friction rub over left chest, abdominal tenderness, fever, albuminuria, pyuria, profound anemia, leucocytosis, N.P.N. 171. Died Nov. 29 with cardiac and renal failure and terminal parotitis.

Autopsy: Chronic cystitis, bilateral hydronephrosis, chronic ureteritis and pyelitis, acute suppurative cystitis and pyelitis. Postmortem blood culture hemolytic streptococci.

CASE 4.—Born 1905. Entered hospital Mar. 18, 1928, for convulsions two days after birth of 7.5 months' fetus. Stuporous, temperature 101.4°, B. P. 186/117, slight edema of face, ankles and retinae, pus, hemolytic streptococci and colon bacilli in catheterized urine, N.P.N. 69. Puerperium febrile. Relapse with fever, headache, and lumbar pain after discharge. May 29, B. P. 160/120. Pleurisy after miscarriage in 1930, led to discovery of hypertension and renal disease. Nov., 1932, after respiratory infection, headache, and bilateral costovertebral pain, diurnal and nocturnal urinary frequency. Feb., 1933, increasing vomiting. Entered hospital Apr. 27, B. P. 170/95, retinal arteriosclerosis, heart failure, albuminuria and pyuria, N.P.N. 181. Persistent vomiting, steady deterioration to death June 1. Convulsion Apr. 30.

Autopsy: Bilateral hydronephrosis and hydroureters, chronic and acute ureteritis and pyelitis, extreme contracted kidneys.

CASE 5.—Born 1889. In seventh month of pregnancy, 1912, chills, vomiting, pain in legs and back, urinary frequency and urgency, hematuria. After this pains and tenderness on one or other side of abdomen or in back. In addition, after 1921, precordial oppression and anginal pain. B. P. 1921, 120/70; 1924, 160/90. 1930, hematuria and pain in both kidney regions. Supravaginal hysterectomy, left oophorectomy, salpingectomy, and appendectomy without relief. 1930, hematuria and bilateral renal pain. 1931, dyspnea, headaches, dizziness, increased urinary frequency, B. P. 265/140, tenderness in right hypochondrium and both lower quadrants, much albumin and few leucocytes in urine, N.P.N. 33. Steady deterioration of cardiac and renal function, with recurrent abdominal and lumbar pain, until death in 1935.

Autopsy: Dilatation of ureters and renal pelves, acute and chronic pyelonephritis, extreme contracted kidneys.

CASE 6.—Born 1892. "Pus on kidneys" in first pregnancy, 1913. Subsequent 3 pregnancies supposedly uncomplicated. 1926, pains in lower quadrants of abdomen. After 1930 increasing headaches and urinary frequency. Nov., 1931, dyspnea, followed later by increasing vomiting, paroxysmal orthopnea and substernal pain. Jan. 10, 1932, developed "grippe," Jan. 17, edema of feet and ankles. Entered hospital Feb. 14 with dyspnea, orthopnea, constant vomiting, anemia, signs of heart failure, B. P. 240/140, retinal scars and hemorrhages, edema of legs and sacrum, tenderness in right lower quadrant, urine of low specific gravity, with albumin, red blood cells, few leucocytes and casts, N.P.N. 198.

Autopsy: Dilatation of ureters and renal pelves, extreme contracted kidneys, acute suppurative pyelonephritis.

CASE 7.—Born 1886. "Kidney trouble" after first pregnancy, 1910. Subsequent attacks of urinary frequency and burning, lasting ten to twenty days, 4 or 5 times a year, with aggravated symptoms during pregnancies in 1914, 1918, and 1920. In eighth month of pregnancy, 1922, edema of ankles, albumin, leucocytes, epithelial cells and casts in urine, without hypertension. Urinary symptoms further aggravated in this pregnancy and another in 1924. Oct. 20, 1926, pain in back, urinary frequency and burning, dizziness, headaches, morning nausea, edema of ankles, B. P. 200/116. Feb. 10, 1927, albumin and leucocytes in urine, B. P. 216/135. Entered hospital Feb. 14 with phenobarbital poisoning (exfoliative dermatitis). Died Mar. 3.

Autopsy: General epithelial desquamation with terminal bronchitis and bronchopneumonia. Bilateral double ureters. Chronic and acute pyelitis with various degrees of dilatation of all four ureters and pelves and extreme secondary contraction of kidneys.

CASE 8.—Born 1894. First pregnancy ended in miscarriage at 6 months; second and third reported uncomplicated. 1916, backache, headache, hematuria, urinary frequency and burning. After this similar attacks at intervals, not relieved by appendectomy and uterine fixation in 1918. Exacerbation of urinary symptoms, dyspnea and blurred vision during pregnancy in 1924. Delivered in March. June 27, B. P. 130/82, symptoms persistent. 1925, edema late in pregnancy. Sept. 27, 1930, B. P. 220/120, albumin, pus, and blood in urine. December, cystoscopy revealed cystitis, bilateral pyelitis, distortion of pelves and calyces of both kidneys, moderate left hydronephrosis, calcareous shadows on right side. Attacks of severe renal pain, frequency, hematuria and increasing signs of heart failure until death, Jan. 26, 1932.

Autopsy: Cystitis, bilateral pyelitis with secondarily contracted pyelonephritic kidneys, right nephrolithiasis.

CASE 9.—Born 1901. Morning nausea and vomiting since childhood. During scarlet fever, 1919, low specific gravity urine with minimal albumin. 1920, vomiting 4 or 5 times a day throughout pregnancy. 1922, dyspnea, choking sensations and nervousness. 1925, hypertension, profuse albuminuria and pyuria discovered. 1927, convulsions after premature delivery. 1928 and 1929, occasional attacks of hematuria with convulsions. Early 1932, severe anemia, frequent epistaxes. Jan., 1933, "grippe" followed by persistent cough and extreme weakness. Entered hospital Feb. 16, semistuporous, dehydrated from vomiting, B. P. 165/94, albuminuric retinitis, enlarged heart, profound anemia, albuminuria and pyuria, N.P.N. 198. Death one month later.

Autopsy: Congenital hypoplasia of urethra and right kidney, bilateral hydro-ureters and hydronephrosis, chronic cystitis, ureteritis and pyelitis with suppurative pyelonephritis on left.

CASE 10.—Born 1901. Two normal deliveries, the second Jan., 1924. Early in March tonsillitis. Mar. 28, right lumbar pain, urinary frequency and burning, hematuria. Entered hospital Apr. 7, B. P. 119/70, both kidneys palpable, tenderness in right flank, temperature 103°, leucocytosis, albumin, pus and streptococci in urine. Cystoscopy Apr. 9 reported negative. June 26, 1925, early in pregnancy, albumin, few leucocytes and few red blood cells in urine, B. P. 94/44. Delivered elsewhere. Entered hospital Oct. 21, 1927, in early pregnancy, vomiting, with slight fever, little albumin, few leucocytes and casts in urine, B. P. 110/60. Entered another hospital Dec. 1, vomiting persisting, with difficulty in voiding, burning on urination, profound anemia, B. P. 115/78, albumin, rare casts and many leucocytes in urine. Death Dec. 3. Autopsy records secured from hospital inadequate.

CASE 11.—Born 1892. May, 1929, early in fifth pregnancy, nausea, vomiting and chills. Comparatively well July and August. Sept 9, pain in back and epigastrium, extreme urinary frequency, edema of feet and face. Sept 23, epigastric and right lumbar tenderness, edema of feet, albumin, occasional leucocytes and rare casts in urine. Pregnancy terminated Sept. 25. Puerperium febrile, complicated by femoral thrombophlebitis, pulmonary embolism, persistent pyuria and bacilluria. 1933, urinary frequency and burning. Cytoscopy May 17, 1934, bifid ureters, right hydronephrosis, N.P.N. 23, phthalein excretion 40. Death few days later from pulmonary embolus following uterine suspension.

Autopsy: Pulmonary embolus. Acute focal necrosis of renal tubules, hemorrhages and congestion of kidneys, some chronic glomerular lesions. Dilatation of right ureter and renal pelvis without pyelitis.

CASE 12.—Born 1896. Normal pregnancies 1925 and 1928, miscarriage 1931. Entered hospital 4 A.M. Dec. 20, almost at term, after 2 months' headache and edema of feet. Pulse 120, B. P. 160/110, edema of trunk and legs, slight cough.

8 A.M. cough worse, sputum bloody, breathing rapid, skin clammy, pulse 144. Signs of bilateral bronchopneumonia at 11 A.M. Death next morning. Albumin, leucocytes and red blood cells in urine, secondary anemia, leucocytosis.

Autopsy: Diffuse bronchopneumonia, extensive hepatic necrosis with inflammatory lesions, slight degenerative changes in renal tubules and glomeruli, dilatation right renal pelvis and ureter without pyelitis.

CASE 13.—Born 1892. First pregnancy terminated at 6 months early in 1924 for severe pyelitis. Later in same year, early in pregnancy, recurrence, treated conservatively. July 6, 1925, slight edema of feet. July 10, epigastric pain and nausea in A.M. Found in coma (presumably postconvulsive) at 4 P.M. Entered hospital, 9 P.M. after 2 more convulsions, with temperature 105°, B. P. 180/100. Blood pressure fell to shock levels after further convulsions. Delivery dead fetus July 7; death July 8, with terminal temperature 107.4°. Much albumin, many leucocytes, red blood cells and bacilli and occasional casts in 2 catheter urine specimens.

CASE 14.—Born 1902. Cesarean section at term for dystocia, 1924: albumin and many leucocytes in urine, blood pressure normal, course afebrile. Cesarean 1926; urine as before, B. P. 138/100, right costovertebral pain and pyuria during puerium. Entered hospital Oct. 11, 1927, with albuminuria, pyuria, edema, retinal edema, bilateral costovertebral tenderness, without hypertension, having had chills, fever and urinary frequency for some time. After cesarean section and section of fallopian tubes, Oct. 21, fever, increasing edema and hypertension. Nov. 13, convulsions, followed by coma and death.

CASE 15.—Born 1897. Pregnancy, 1925, presumably uncomplicated. Early in Dec., 1932, in seventh or eighth month, sore throat, hoarseness and cough, with later increasing nausea, vomiting, and epigastric pain. Entered hospital Jan. 2, 1933, vomiting, dehydrated, afebrile, with slight cervical adenitis, minimal icterus and edema, B. P. 130/90, extensive retinitis, many leucocytes and bacilli, but little albumin and rare casts in urine. Cesarean section Jan. 17. Death Jan. 27, preceded by fever, increasing to 104°, and terminally by nystagmus, strabismus, signs of tetany, left facial weakness and convulsions, but no hypertension.

CASE 16.—Born 1889. 1914, pyelitis. Recurrence 1918 and 1920, when cystoscopy confirmed diagnosis (bilateral), B. P. 118/70, phthalein excretion 78. 1922, after delivery, hematuria, fever and lumbar pain. Feb., 1925, dizziness, blurred vision, vomiting, weakness, fever and extreme urinary frequency. Entered hospital Mar. 1 after 2 convulsions, B. P. 200/150, advanced retinitis, albumin, casts and pus in urine, N.P.N. 53. Increasing renal and cardiac failure until death, June 8, 1926.

CASE 17.—Born 1888. Oct. 5, 1926, delivered at term after a week of hypertension without albuminuria. Oct. 6, sudden convulsion followed by sudden passage of large volume of urine. B. P. 230/160. Puerperium febrile, with persistent hypertension, urinary frequency and burning and profuse pyuria. History of cystitis preceding pregnancy. Cystoscopy Mar., 1927, cystitis and right pyelitis. Symptoms of urinary infection and hypertension until death from cerebral accident Mar. 29, 1933.

CASE 18.—Born 1892. Dec. 24, 1922, 4 months before term in third pregnancy entered hospital for hemorrhage from separated placenta, with albuminuria, cylindruria and B. P. 168/122. Pregnancy terminated. Puerperium febrile, hypertension persistent. Entered hospital Sept. 12, 1923, 3 months before term, with lumbar pain, headache, B. P. 250/150, retinal edema and cardiac enlargement. Supravaginal hysterectomy. Puerperium febrile. Hypertension, pyuria and pains in back persisted. 1927, hemiplegia. Bilateral hydronephrosis and pyelitis proved by cystoscopy. Death June 1, 1928, from intraventricular hemorrhage.

CASE 19.—Born 1887. 1907, in third month of first pregnancy, albuminuria and edema. Ill for a month following termination of pregnancy. 1914, entered hospital for similar condition. Aug. 29, 1923, in eighth month B. P. 154/94; Sept. 14, 160/100, albuminuria and pyuria. After delivery, Sept. 20, persistent hypertension and pyuria with pain in back. Oct., 1925, swelling of face, pallor and epistaxis, succeeded in December by dyspnea, nausea and vomiting. Entered hospital Dec. 17 *in extremis* with advanced renal and cardiac failure and died Dec. 19. N.P.N. 410.

CASE 20.—Born 1895. 1925, miscarriage. Burning urination 1 week in succeeding summer. Mar. 9, 1926, in third month, symptoms of pyelitis. April 14, cystoscopy revealed pus from left ureter, dilatation of left renal pelvis and impaired function of both kidneys. Treatment by renal lavage until July 29. Sept. 25, B. P. 150/90, rising to 172/90. Entered hospital Oct. 9, 3 P.M., vomiting, 6 P.M. convulsions, delivery 10:30. Puerperium febrile. Hypertension subsided. Cystoscopy, Mar., 1927, persistent left hydronephrosis, impaired function right kidney, unimproved by cystoscopic treatments and plastic operation on left renal pelvis.

CASE 21.—Born 1903. Entered hospital Oct. 15, 1935, at term. Symptoms of pyelitis early in pregnancy, febrile illness in August, edema leading to discovery of pyuria in September, followed by increasing hypertension and albuminuria. Oct. 18, cesarean section, followed by prolonged fever, renal pain and urinary frequency and burning, complicated by pleurisy with effusion. Nov. 7, intravenous pyelograms revealed right hydronephrosis and hydroureter. Pyuria persisted 2 months later.

CASE 22.—Born 1900. Entered hospital Jan. 7, 1928, 6 months pregnant with bilateral pyelitis, hydronephrosis and hydroureters (cystoscopic diagnosis), N.P.N. 43, phthalein excretion 50. Discharged and delivered at home. Readmitted Aug. 13, 1929, 3 months pregnant, with symptoms and signs of pyelitis and history of intermittent hematuria since previous pregnancy, B. P. 100/60. Pregnancy terminated by hysterectomy. Treatment in urologic clinic until Apr., 1932.

CASE 23.—Born 1899. Nov., 1920, in first pregnancy, pain in left side, urinary frequency and burning. Entered hospital March 20, 1921, B. P. 160/120. April 1, cystoscopy revealed severe cystitis (ureters and kidneys not examined). After delivery April 2, fever, unmistakable signs and symptoms of pyelitis, *B. coli* in urine. B. P. 140/95 on discharge, April 13.

CASE 24.—Born 1904. Dec. 2, 1929, 5 months pregnant, sore throat, cough and chills; Dec. 7, pain and tenderness in right flank, radiating downward, urinary frequency and burning, herpes, albumin, pus and blood in urine, B. P. 138/70, N.P.N. 35. Cystoscopy revealed bilateral pyelitis, *B. coli*. Cesarean section Jan. 10. Subsequent treatment in urologic clinic. Jan., 1933, urine negative, B. P. 120/74.

CASE 25.—Born 1902. 1918, pneumonia. Jan., 1924, scarlet fever, treated with serum, complicated by serum sickness and pyuria. Nov., 1924, curettage for incomplete abortion, B. P. 130/70, few leucocytes and red blood cells without albumin in urine. June, 1925, similar condition, slight albuminuria. Feb. 15, 1927, 7 months pregnant, B. P. 153/94, tenderness in both flanks, general edema, leucocytes and *Staph. aureus* in catheterized urine. Difficulty in voiding and pain on urination earlier in pregnancy. Delivered March 3, puerperium febrile. April 10, 1930, premature delivery after a week of vomiting, edema, albuminuria, B. P. 170/116, albumin, leucocytes and *B. coli* in urine. May 17, cystoscopy revealed cystitis, but no pyelitis. Sept. 29, renal lavage for *B. coli* pyelitis. May 21, 1931, pregnancy terminated after symptoms of pyelitis, because of edema, B. P. 200/130, chorio-

retinitis. May 3, no hydronephrosis by intravenous pyelography. Section of fallopian tubes June 13. Followed until Aug. 21, 1935, for dyspnea and palpitation without hypertension.

CASE 26.—Born 1890. Kidney trouble 1 month in first pregnancy, 1917. June 23, 1919, in last month of pregnancy, bilateral pyelitis of 2 months' duration diagnosed by cystoscopy. Delivered July 14, B. P. normal. Aug., 1927, early in pregnancy slight albuminuria without hypertension. Delivered Mar., 1928. Blood pressure, determined only at time of discharge, 110/70. April 23, B. P. 140/96, slight albuminuria. Still surviving Jan. 8, 1931.

CASE 27.—Born 1898. Cesarean section, 1928, for premature separation of placenta and albuminuria. 1930, cesarean at term for albuminuria and edema, B. P. 112/70, followed by ulcerative cystitis, treated until Feb. 10, 1934. No examinations of kidneys nor blood pressure.

CASE 28.—Born 1915. 1928, cellulitis of leg and urinary frequency. Sept., 1933, fibrosarcoma of right axilla removed, B. P. 132/88, minimal albumin and many leucocytes in urine. Oct. 15, 1935, near term, B. P. 156/110, albuminuria, edema of hands. Nov. 23, after delivery, right hydronephrosis and hydroureter by intravenous pyelography. Jan. 30, 1936, same by cystoscopy.

CASE 29.—Born 1918. Nov. 26, 1935, just before term in first pregnancy, after a month of slight edema, slight albuminuria, B. P. 146/95. Delivered Nov. 30. Dec. 7., mild right hydronephrosis by intravenous pyelography.

CASE 30.—Born 1897. 1917, second pregnancy terminated for hypertension, pain in back and sides, without albuminuria. Subsequent intermittent pain in flank. From August to December, 1920, headache, pain in back and hypertension. Sept., 1922, delivered at home, no albuminuria nor hypertension in August. Entered hospital Sept. 24, 1923, for chills, fever, urinary frequency and burning, with profuse pyuria, B. P. 170, phthalein excretion 45. Cystoscopy revealed cystitis and left pyelitis. Feb., 1925, after self-induced abortion at 5 months, albuminuria and pyuria. Nov., 1929, in sixth month B. P. 170/100. Dec., urinary frequency, dyspnea, edema of ankles, B. P. 200/100, N.P.N. 23, phthalein excretion 65. Urethral stricture, chronic cystitis and dilatation of both renal pelves found by cystoscopy. Stricture dilated. Delivered Mar. 10, 1930. Treated for hypertension and cardiac asthma until June, 1933.

CASE 31.—Born 1882. 1909, after stillbirth (third pregnancy) at term, pyelitis discovered. 1922, sharp pain in right flank. Oct., 1924, after similar pain in left flank cystoscopy revealed calculus at left ureteropelvic junction, dilatation of left renal pelvis, coeci and pus from both ureters. B. P. 178/100, heart enlarged. Calculus removed by pyelotomy. Increasing hypertension and associated symptoms until last visit, Apr., 1934.

CASE 32.—Born 1905. 1923, pregnancy terminated in fifth month for bilateral pyelitis. Chills, fever and pyuria in puerperium. Subsequently subcutaneous abscesses and blood culture containing nonhemolytic streptococci and *Staph. aureus*. Bilateral hydronephrosis found at cystoscopy. In subsequent pregnancies in 1928, 1933, 1934, and 1935, increasing signs of hypertension and heart failure with angina. Dec., 1935. B. P. 200/130, albumin and leucocytes in urine, N.P.N. and phthalein normal, moderate right hydronephrosis and hydroureter by intravenous pyelography.

CASE 33.—Born 1906. Kidney trouble 1908. Mar. 27, 1927, in fourth month of first pregnancy, pyuria, following tonsillitis, with chills and fever, treated elsewhere. Apr. 24, pyuria, B. P. 120/75, N.P.N. 32, phthalein excretion 60. May 27,

edema of feet. June 5, B. P. 148/88. July 31, disturbance of vision, B. P. 150/100. Aug. 5, during labor, convulsions. Puerperium febrile. Aug. 21, on discharge, pyuria persisted.

CASE 34.—Born 1905. Feb., 1927, early in first pregnancy pain in right flank, chills, fever, urinary frequency and burning. June 28, signs of acute pyelitis, fever, nonhemolytic streptococci in blood culture, no hypertension. July 13, perirectal abscess drained. Delivered elsewhere Oct. 3. 1928, miscarriage at 7 months. 1929, delivered elsewhere, fever and pyuria in puerperium. 1932, seen once in pregnancy at 3 months, condition unknown.

CASE 35.—Born 1893. 1923, 2 months after second delivery, urinary urgency, frequency and burning. 1927, increasing frontal headaches, 1928, pain in back, failing vision, followed later by palpitation, dyspnea, vomiting and frequent epistaxes. 1929, pus and *B. coli* in urine, advanced retinitis, B. P. 270/150, N.P.N. 33, phthalein excretion 40.

CASE 36.—Born 1900. 1928, in last month of pregnancy, albuminuria and pyuria. Ten days later slight retinal edema, B. P. 130/100, N.P.N. 26, phthalein excretion 60, *B. coli* in catheterized urine. Two weeks later, at term, edema of feet and ankles, puffiness of eyelids, retinitis. After delivery, fever, suprapubic pain and urinary frequency. Pyuria a month later. B. P. not elevated except as noted above.

CASE 37.—Born 1885. 1921, in fifth pregnancy terminated for hematuria, urinary frequency, headaches and palpitation. 1924, abortion at 2 months. Jan. 1, 1925, in fourth month, headache, epistaxis, urinary frequency, dyspnea, palpitation, B. P. 250/140. N.P.N. Feb. 11, 96, Feb. 20, 120; phthalein excretion 6, albumin, pus, blood and casts in urine. Left hospital against advice.

CASE 38.—Born 1896. 1929, early in first pregnancy, urinary frequency and burning with pyuria. Six weeks before term slight hypertension and edema. Recurrence of dysuria just before term. Febrile puerperium.

CASE 39.—Born 1905. Entered hospital in first labor Feb. 14, 1927, with edema of legs, B. P. 160/100, after period of edema, visual disturbances, urinary frequency and burning. Puerperium febrile, with pus in catheterized urine. May 9, backache, urinary frequency and burning and profuse pyuria, which had disappeared by June 25.

CASE 40.—Born 1895. 1925, kidney trouble in fifth month of pregnancy, but went to term. Renal condition and blood pressure aggravated during puerperium. Early in Jan., 1927, 4 months before term, increasing edema. Entered hospital Feb. 9, with general edema, retinitis and hypertension. After delivery Feb. 10, high fever, urinary frequency and burning, abdominal pain, bilateral costovertebral pain and pyuria.

CASE 41.—Born 1874. 1910, in second month of second pregnancy bilateral costovertebral pain and urinary burning. After delivery at term, convulsions, delirium, fever and urinary retention. Subsequently albuminuria and frequency. 1924, hypertension. 1926, headaches and edema of ankles. 1929, B. P. 184/100, heart enlarged, retinal arteriosclerosis. Steadily increasing hypertension with cardiac and renal failure until last seen in 1935 with B. P. 210/100, heart failure, fever, costovertebral tenderness, pus and *B. coli* in catheterized urine, N.P.N. 45 to 60.

CASE 42.—Born 1898. Mar. 24, 1926, albuminuria, B. P. 200. Delivered Apr. 5. Puerperium febrile with hypertension until Apr. 24, and frank pyuria throughout. June 11, B. P. 150/95, many leucocytes in urine. Mar., 1932, B. P. 140/88, urine clear.

We should like to express our appreciation to Dr. Arthur H. Morse, to whose kindness in providing the material and his cooperation in the investigation we are greatly indebted.

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BLOOD AND PLASMA VOLUME CHANGES IN ECLAMPSIA*

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MARKED changes in many of the constituents of the blood occur during pregnancy. These changes in the blood and plasma volumes, hemoglobin and serum protein concentration are of such a magnitude that if the patient were not pregnant they would be considered abnormal and might be associated in many cases with characteristic symptoms and signs. Such alterations in blood volume in eclampsia and preeclampsia are intimately associated with the disease process.

During the past twelve years we have been studying various constituents in the blood and urine of toxemic patients. As soon as sufficient data were accumulated for one substance its determination was stopped, unless significant changes occurred. Thus during this period innumerable analyses were made, but the most marked changes, which were detected by frequent serial specimens of blood and which were of prognostic value, were in the hemoglobin, cell volume, and serum protein concentration in eclampsia and preeclampsia. These changes which may occur with extreme rapidity in many patients are due to alterations in blood and plasma volumes.

Table I illustrates the average and range for the hemoglobin, cell volume, and serum protein in patients with eclampsia. The day on which the convulsions and coma occurred is designated as "O," and the data are listed under days before

*Read by invitation at Duke University, Durham, North Carolina, April 23, 1936.

TABLE I. BLOOD CHANGES IN ECLAMPSIA

PER CENT—AVERAGE	NO. OF DAYS BEFORE ECLAMPSIA				NO. OF DAYS AFTER ECLAMPSIA							
	2	1	0*		1	2	3	4	7	14	21	90
Hemoglobin†												
Range	87	96	108		95	93	97	89	84	84	93	103
No. of patients	71-95	83-129	74-154		53-154	63-125	68-118	65-125	59-118	59-119	65-125	95-112
	4	7	34		30	22	12	13	18	23	14	7
Cell volume												
Range	41	41	45		37	37	38	35	34	35	37	41
No. of patients	31-49	32-48	35-57		27-51	27-50	28-46	24-52	23-50	25-45	27-42	36-46
	5	13	42		33	25	14	13	26	26	14	10
Serum protein												
Range	5.7	6.0	6.7		5.3	5.4	5.1	5.4	6.0	6.7	6.8	7.2
No. of patients	5.5-5.8	4.8-7.4	5.1-8.4		3.8-8.0	3.9-6.9	3.7-7.3	4.4-6.7	4.8-8.4	5.1-7.8	5.9-7.5	6.6-7.7
	2	17	41		31	26	15	10	22	25	14	9

*0 = day of eclampsia.

†100 per cent hemoglobin = 13.8 gm. hemoglobin.

and after the occurrence of the acute disease. These studies were made on 97 patients with eclampsia, but a sufficient number of serial determinations were obtained on only 42. The convulsions and delivery occurred on the same day in 34 patients. Five patients had eclampsia two to nine days before, and three after delivery. The reduction in the concentration of hemoglobin, cell volume and serum protein without hemorrhage indicates an increase in blood and plasma volumes. An increase in the concentration indicates a shrinkage in the volume. These changes are not always parallel, but the direction of change is usually the same. Thus, for example, in one patient the hemoglobin dropped 37 per cent, the cell volume 34 per cent, and the serum protein only 25 per cent. The maximum average decrease in serum protein, amounting to 24 per cent, occurred on the third day and then there was a rapid return to the normal range by the fourteenth day. The maximum hemoglobin and cell volume reductions occurred on the seventh day and amounted to 22 and 25 per cent, respectively. By the third postpartum week the hemoglobin and cell volume concentrations were within the normal range. The increase in serum protein is slightly more rapid than in the hemoglobin and cell volume. Similarly, the increase in cell volume is more rapid than the hemoglobin. Occasionally, when a blood dilution occurs, the discrepancy between hemoglobin and cell volume is so great it gives the appearance that red blood cells were introduced, which contain a higher concentration of hemoglobin than that originally present.

Serial determinations of blood and plasma volumes were made, but, unfortunately, with the methods now available repeated determinations at short intervals do not give reliable results. Our average figures are listed in Table II. The difference in blood and plasma volumes between the normal pregnant and preeclamptic group is not significant. The number of eclamptic patients is too small to be of value. It is obvious, however, that both groups, especially the latter one, show a definite decrease in blood volume. Rowntree and Brown designate this condition as a polycythemic hypovolemia (a decrease in both blood and plasma, but a greater

TABLE II. VOLUME PER KILOGRAM OF BODY WEIGHT

	NO. OF PATIENTS	BLOOD—C.C.		PLASMA—C.C.	
		AVERAGE	RANGE	AVERAGE	RANGE
Nonpregnant women*	25	85.7	77-94	51.7	45-58
Normal pregnancy	55	80.9	55-115	49.8	35-65
Vascular-renal disease	29	83.2	69-105	50.9	45-65
Preeclampsia	14	77.5	65-95	47.0	35-55
Eclampsia	6	71.4	67-78	39.4	33-46

*Rowntree, L., and Brown, G.: *The Volume of Blood and Plasma*, Philadelphia, 1929, W. B. Saunders Co.

decrease in the latter than the former, resulting in a proportionally greater cell volume). Three of the eclamptic patients with the small blood volumes died.

Fig. 1 illustrates graphically the changes in hemoglobin, cell volume, and serum protein which occurred before, during, and after eclampsia in three patients. The first patient, E. R., who had a severe preeclampsia with a subnormal blood and plasma volume, showed an increase in the hemoglobin, cell volume, and serum protein of 12, 21 and 28 per cent while under treatment, or an average reduction in the blood volume of 20 per cent. The blood pressure increased, the urine volume decreased, and headache and visual symptoms appeared simultaneously. Labor was induced, but within a few hours convulsions and coma developed. Coma was still present forty-eight hours after delivery and the patient regained consciousness only after an injection of gum acacia solution which initiated a blood dilution, a diuresis and clinical improvement. If the blood and plasma volumes at

the sixth postpartum week were normal for this patient, whose weight was 14 kg. less, then the volumes determined before the convulsion were markedly below normal.

The second case illustrates the reduction in hemoglobin, cell volume and serum protein, or an increase of blood volume amounting to 18 per cent, coincidental with the cure of the convulsions and coma seven days before delivery. Our treatment consisted of intramuscular injections of 25 per cent magnesium sulphate and intravenous injections of 1000 c.c. of 20 per cent glucose solution at six- to eight-hour intervals.

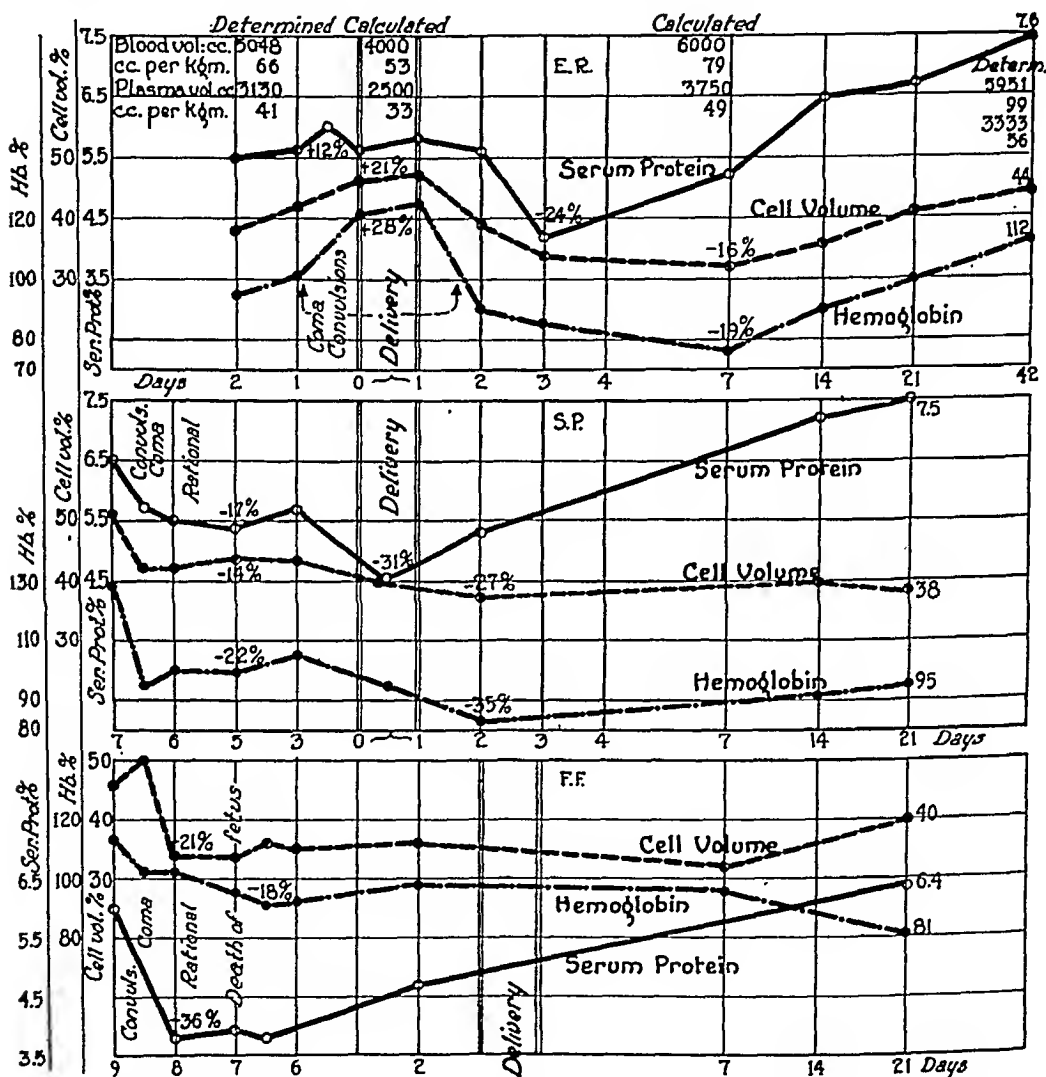


Fig. 1.—Graphs illustrating the plasma and blood volume changes which occurred in three patients with eclampsia.

The third case, F. F., also illustrates the blood dilution which occurred simultaneously with the cessation of convulsions, return of consciousness and diuresis. The fetus died forty-eight hours after admission of the patient. The calculated average increase in blood and plasma volumes amounted to 23 per cent.

Table III lists the average changes in blood and plasma volumes as determined by changes in hemoglobin, cell volume and serum protein. The figure for the initial determinations was used as the divisor and the difference between it and the figure for the greatest increase or decrease was the dividend. The quotient was multiplied by 100. The three quotients were added together and an average figure

was obtained. This figure was assumed to represent the alteration in blood volume. If the hemoglobin, cell volume and serum protein increased, the blood and plasma volumes decreased, and vice versa.

Column (a) represents those patients in whom one or more blood specimens were obtained two hours to seven days before the onset of convulsions. Twelve patients showed a reduction in blood volume of from 7 to 46 per cent, as convulsions and coma occurred. These patients showed comparable increases in volume after delivery, as indicated in Column (b).

TABLE III. BLOOD VOLUME CHANGES IN ECLAMPSIA

RANGE OF CHANGE PER CENT	PREECLAMPSIA → ECLAMPSIA		ANTEPARTUM OR POSTPARTUM ECLAMPSIA	AFTER INTRAPARTUM ECLAMPSIA AND DELIVERY	
	ANTEPARTUM	POSTPARTUM		DECREASE	INCREASE
	DECREASE	INCREASE	INCREASE		
	(a)	(b)	(c)	(d)	(e)
1-9	5			2	2
10-19	2	3	4	1	11
20-29	2	3	4		9
30-39	2	5			3
40-49	1				
Total	12	11	8	3	25

Column (c) contains data from eight patients, five of whom had antepartum, and three postpartum, eclampsia. The convulsions in the former group occurred 2, 6, 7, 9, and 9 days, respectively, before delivery. There was no blood loss in this group. The changes in volume in the postpartum group resemble those of the antepartum group so closely that we do not believe they were due to the blood loss of 200 to 300 c.c. occurring at the time of delivery.

Columns (d) and (e) contain data from patients in whom the onset of the eclampsia preceded the delivery, but both occurred on the same day. Three patients showed a further decrease in blood volume while under treatment. Two of them died. After delivery the increase ranged from 7 to 39 per cent.

Blood studies were available in three patients who died. They showed average decreases in the blood volume as follows: 11, 17, and 14 per cent. The amount of blood in three of these was 69, 78, and 69 c.c., and the plasma was 39, 39, and 32 c.c. per kilogram of body weight.

Fig. 2 illustrates the changes in cell volume and serum protein during normal and toxemic pregnancy. Dieckmann and Wegner have demonstrated, by serial determinations of blood and plasma volumes, hemoglobin, cell volume, and serum protein concentration on the same patients, that the increase in plasma volume is 25 per cent and the blood volume is 23 per cent at term. Therefore, although there is a decrease in the concentration of hemoglobin, cell volume, and serum protein, the total amount of each is increased. No adequate explanation for these changes has been advanced. In a previous article, using similar methods, the author demonstrated that the changes in the concentration of hemoglobin, cell volume, and serum protein in the vascular-renal group (chronic nephritis in pregnancy) were parallel to those of normal pregnancy. However, preeclamptic patients showed changes similar to those of eclampsia. The fact that the graphs for these latter two conditions are almost identical indicates the close relationship of preeclampsia to eclampsia. The cerebral, visual, and gastrointestinal symptoms, and the oliguria of preeclampsia and eclampsia are directly associated with the blood concentration. The amelioration or cure of these symptoms likewise occurs with a blood dilution. The height of the blood pressure, degree of albuminuria, or amount of edema does not always parallel the changes in blood volume.

DISCUSSION

The increase in hemoglobin, cell volume, and serum protein is caused by the passage of water as a dialysate containing electrolytes, glucose, and the nonprotein nitrogen constituents into the tissues. Serum protein escapes into the tissue spaces and some of the erythrocytes may be stored in the spleen and others stagnate in the capillaries of the muscles if the blood concentration is prolonged. The reverse process occurs as the blood dilutes, and water, electrolytes, etc., pass into the blood stream. A blood dilution occurs after hemorrhage. If the reduction in the hemoglobin, cell volume, and serum protein occurred only after delivery the most probable explanation would be that it is the result of the blood dilution taking place after the blood loss incidental to delivery. The fact that a blood dilution was observed five

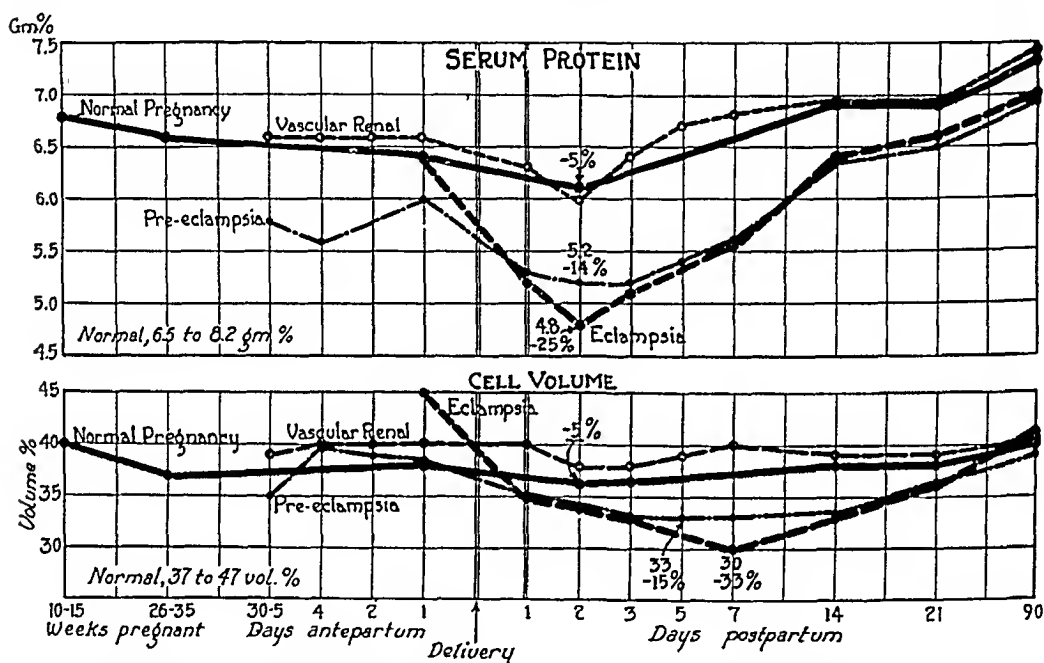


Fig. 2.—Graphs illustrating the average changes as determined by serial examinations of the blood. The figures for eclampsia are based on 21 eclamptic patients, and differ slightly from those in Table I, which are based on 42 patients.

times before delivery indicates that hemorrhage is not a factor. Furthermore, the blood was more concentrated in fifteen cases, thus indicating the need for a subsequent dilution or return to the normal. The hemoglobin, cell volume, and serum protein concentration may drop below the normal because of an overcompensation by the vascular system, but the normal volume is established within a few days. There is no constant relationship between the degree of blood dilution and the amount of edema.

The observations of Rowntree and Brown on patients, and Dieckmann and Wegner on themselves and patients, demonstrate that the blood and plasma volumes, hemoglobin, cell volume, and serum protein concentration tend to be constant for the individual under normal

conditions. Disease or markedly abnormal practices, such as the excessive ingestion of water, deliberate dehydration, or excessive exercise, will cause changes, but as soon as conditions are normal, the hemoglobin, cell volume and serum protein, and in all probability the blood and plasma volumes, return to their usual amount.

The blood dilution which occurs after delivery in toxemic patients was discussed by Schwarz and Dieckmann in 1929, with a review of the literature. They demonstrated that clinical improvement in eclampsia was associated with a blood dilution. Failure of the blood to dilute with their usual treatment indicated that the eclampsia was of the severe type and that delivery offered the only hope for the mother.

Skajaa determined the cell volume of a large number of normal and toxemic patients and reported his results in 1929. He stated that an average blood concentration of 15 per cent, or condensation, as he termed it, occurred during labor in toxemic patients. Those patients showing a greater concentration also evidenced symptoms of greater severity in the toxemias. Blood dilution was accompanied by abatement of the symptoms. He stated that the greatest condensation was found in impending eclampsia, amounting to 23 per cent before labor and to 30 per cent during labor. The average blood dilution amounted to 25 per cent during convalescence. One patient showed a 78 per cent decrease in cell volume.

The reports by Skajaa and by Schwarz and Dieckmann were published independently of each other in 1929. The results and conclusions are identical.

Table IV contains data from a group of diseases which are associated with a blood concentration. It has been only within the past decade that the clinician has become cognizant of the importance of a concentration of the blood. The data in the table indicate that the amount of fluid usually given parenterally, necessary to restore the blood and plasma volumes to normal, ranges from 93 to 843 c.c. per hour. It is obvious that the administration of small amounts of fluid is of little value. The treatment of these various conditions necessitates the regulation of the water balance by the determination of hemoglobin, cell volume, or serum protein, or by the hourly measurement of the urine. The latter plus one of the blood constituents is the ideal method.

It has been demonstrated repeatedly that shock is associated with a hemoconcentration, but the results of Underhill and coworkers in the treatment of severe burns with large amounts of fluid first indicated the clinical importance of reduction in blood volume. They demonstrated conclusively that the hyperpyrexia, tachycardia, delirium, oliguria, and high mortality in extensive burns was associated with a tremendous increase in hemoglobin concentration, indicative of a blood concentration, but that if sufficient fluids were given to lower the hemoglobin to normal, these symptoms and signs disappeared or were abated in degree and recovery usually occurred.

Peters and coworkers, Ralli and Waterhouse, and other investigators have described the concentration of the blood in diabetic coma, as indicated by the high hemoglobin, cell volume or serum protein concentration, compared with the figures for these substances when the diabetes is under control. They noted that an oliguria or anuria was present with the concentrated blood. If urine could be obtained, it contained remarkably low concentrations of nitrogen and sodium chloride. The concentration of these substances in the urine increased rapidly as the condition of the patients improved and the blood became diluted. We have made similar observations in eclamptic patients. They have pointed out that there is no parallelism between hemoglobin and serum protein changes, but that the direction of change is the same. They also noted that a failure of the blood to dilute or a reappearance of the blood concentration indicated a change for the worse in the clinical condition. They stated, furthermore, that a delay in the restoration of serum volume and blood concentration is a more accurate criterion for determining the prognosis than either blood sugar or carbon dioxide determination.

Himwich has demonstrated that the lack of water in depancreatized dogs causes a blood concentration, as evidenced by increased specific gravity, osmotic pressure and hemoglobin concentration. The administration of water cures the various symptoms and signs. The result of these changes, as depicted by him and to which we have made certain additions, is as follows:

DECREASED BLOOD VOLUME

Decrease in blood supply to skin → Hyperpyrexia

Decrease in blood supply to muscle → Lactic acid

Decrease in blood supply to kidney → Nitrogen and acid retention

Increase in blood viscosity → Additional work for heart → Tachycardia →

Myocarditis

Changes in EKG similar to those of insufficient oxygen supply to heart.

Marked reductions in blood and plasma volumes are associated with cholera, the anhydremia of babies, and severe protracted vomiting from any cause. The administration of adequate amounts of fluid usually causes marked improvement in the disease. Bilateral adrenalectomy in the dog results in a blood concentration which can be cured by the parenteral administration of extract of the adrenal cortex.

Friedlander, Silbert and Laskey have stated in several reports (1) that the blood volume is decreased after thyroidectomy or oophorectomy in the experimental animal; (2) oophorectomy in a young woman is distinguished by a decrease in blood volume; (3) that the blood volume is decreased in thrombo-angiitis obliterans; and (4) that the administration of thyroid extract will cause an increase in it. Thompson noted a 23 per cent increase in the plasma volume of patients with myxedema

following the administration of thyroid extract. There appears to be some relation between blood and plasma volumes and diminished function of the adrenal and thyroid glands and the ovaries. While it is tempting to theorize on the regulation of blood volume by one of these glands, it is obvious that many more observations must be made before any conclusions can be drawn.

CONCLUSIONS

1. A concentration of the blood, which may be relative (below the average for the period of pregnancy) or absolute (less than the normal for the nonpregnant patient), occurs in eclampsia.

2. This concentration can be demonstrated by blood and plasma volume determinations, but it is best demonstrated by serial determinations of hemoglobin, cell volume, or serum protein concentration. The change in concentration of these substances is not always parallel, but the direction of change is usually the same.

3. A concentration of the blood and plasma is not the cause of the eclampsia, but it is intimately associated with the convulsions, coma, oliguria, and the various cerebral, visual, and gastrointestinal symptoms. A blood dilution is associated with clinical improvement as determined by a diuresis, cessation of the convulsion, return to consciousness, decrease in temperature, pulse, etc.

4. Death occurred in three patients in whom a permanent blood dilution could not be maintained.

5. Since the exact cause of eclampsia is unknown and a concentration of the blood occurs which may be so marked as to be incompatible with life, treatment which will dilute the blood should be instituted. Innumerable methods of treatment have been used. If the case is mild almost any type of treatment, provided it carries no mortality of its own, is efficacious. If the case is severe, treatment which comprises control of the convulsion, dilution of the blood, and relatively early delivery must be instituted.

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BLOOD LIPIDS IN PREECLAMPSIA*

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IT HAS been previously shown in this JOURNAL¹ that the convulsive and preconvulsive stages of eclampsia are characterized by a significant increase in the ratio of phospholipid to total cholesterol values of blood plasma. At that time it was intimated that a further study of this relationship was being made in cases diagnosed as preeclampsia in an effort to determine if this ill-defined condition could be subdivided on the basis of the plasma P/TC ratio. The present report is concerned with blood lipid findings in 49 cases of preeclampsia. Previous literature on this subject has been covered in the former communication.¹ Professor H. Kürten of Munich has kindly informed the author that he had already suggested that lipid ratios were of significance in the toxemias of pregnancy and eclampsia in a paper published in 1924.²

The present series of cases were of severe or relatively severe preeclampsia. The patients exhibited hypertension, albuminuria and edema all of considerable extent. In addition many complained of headaches, visual disturbances, and oliguria. Renal function tests (phenolphthalein excretion, urea clearance, polyuria, etc.) occasionally indicated some impairment of renal activity but the results were not consistent. Likewise the usual blood chemistry findings were of a variable nature (urea, uric acid, creatinine, sugar, carbon dioxide, etc.). All patients were at or near the termination of pregnancy, and there was no history or other evidence of chronic nephritis in the group herein reported. Mild toxemias with slight hypertension or albuminuria have not been included in this series, although in incidence they comprised about an equal number to the more severe cases and most of them, for the lack of data to the contrary, were diagnosed as preeclampsia.

An oxalated specimen of blood was obtained in the morning usually under fasting conditions. All patients were hospitalized at the time blood was taken, and under these conditions breakfast does not appreciably affect plasma lipid values of normal persons,⁴ but there may be a slight difference in the values of the red blood cells.⁵ Potassium oxalate as an anticoagulant tends to dilute plasma resulting in about 10 per cent lower values for the lipids⁶ but oxalated blood was used in the previous studies of normal pregnancy and eclampsia with which it was desired to

*Received for publication, May 7, 1936.

This work was aided financially by the Alice F. Richardson Fund of the Kingston General Hospital, and was begun while the author was associated with the University of Rochester School of Medicine and Dentistry, Rochester, N. Y.

compare the present results. Extracts of plasma and of the red blood cells were prepared and each was analyzed by the author's modification of Bloor's oxidative microtechnic.^{7, 8}

When the cases were considered collectively by means and standard deviations, there appeared to be no significant variations from the corresponding values for normal pregnancy.³ Since the significant variation found in eclampsia was an increase in the plasma P/TC ratio, a frequency distribution curve of this value in preeclampsia was prepared. This is shown in Fig. 1. It is obvious that there are two peaks in the distribution and that it is possible to construct two frequency curves. This indicated that there were two types of cases in the preeclamptic

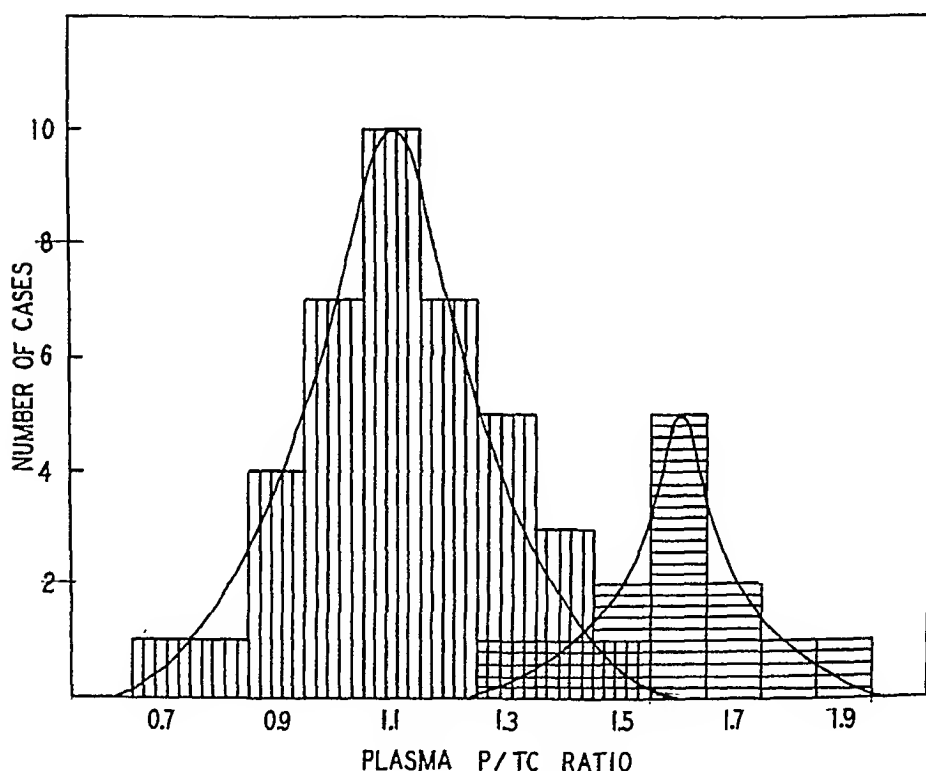


Fig. 1.—The frequency distribution of values for the plasma P/TC ratio in 49 cases of preeclampsia.

group, one having a relatively normal plasma P/TC ratio and another smaller group in which the ratio was elevated as in eclampsia.

An arbitrary ratio value of 1.5 was taken as the dividing line and the cases tabulated into two groups according to whether their ratio was above or below 1.5. It is recognized that a few cases of the lower ratio group might have values above 1.5 in a large series and that a few cases of the higher ratio group might be below 1.5. To be on the safe side when a question of therapy is involved, the author advises the use of 1.4 as the lower limit for potential eclamptics since values in the 1.4 class have been found in eclampsia.¹ The value of 1.5 was selected now since it was desired to compare lipid values for plasma and the red blood

cells in the two groups and 1.5 appeared to be the nearest delineation statistically. The value of the ratio depends, of course, upon the methods used for phospholipid and total cholesterol, but it would appear possible to employ methods other than those used by the author, providing the normal range and the range in the two groups of preeclampsia be first established.

A comparison of plasma lipid values in the normal and high ratio groups of preeclampsia is given in Table I. The complete tabulation of all values would require the presentation of some one thousand figures,

TABLE I. AN ANALYSIS OF THE LIPID VALUES FOUND IN BLOOD PLASMA IN PREECLAMPSIA; THE RESULTS ARE EXPRESSED IN MG. PER 100 C.C. OF PLASMA

VALUE	TOTAL LIPID	COMPOSITION OF TOTAL LIPID						LIPID RATIOS		
		NEUTRAL FAT	TOTAL FATTY ACIDS	CHOLESTEROL			PHOSPHO-LIPID	P/TC	P/FC	P/EC
				TOTAL	ESTER	FREE				
Normal Ratio Group (38 Cases)										
Minimum										
Total lipid	655	126	365	211	148	63	219	1.04	3.48	1.48
Maximum										
Total lipid	1380	553	910	322	211	111	364	1.13	3.28	1.72
Mean values	953	342	613	235	162	73	268	1.14	3.67	1.65
Standard deviation	208	122	171	49	46	16	55	0.17	0.58	0.12
Standard deviation in per cent of mean	22%	36%	28%	21%	28%	22%	21%	15%	16%	7%
High Ratio Group (11 Cases)										
Minimum										
Total lipid	840	97	482	213	161	52	422	1.98	8.10	2.62
Maximum										
Total lipid	1350	382	742	321	205	116	510	1.59	4.40	2.49
Mean values	990	352	651	206	127	79	347	1.68	4.40	2.73
Standard deviation	181	183	128	58	51	24	80	0.26	0.79	0.74
Standard deviation in per cent of mean	18%	52%	20%	28%	40%	30%	23%	16%	18%	27%

and hence a statistical method has been employed. The formula used for calculating the standard deviation has been previously given in this JOURNAL.¹

It may be seen from Table I that there were no marked differences in the plasma lipid values between the two types of preeclampsia. The high ratio group tended to have higher values for all lipids except ester cholesterol which was low and consequently produced a low total cholesterol. Along with this tendency to a low ester cholesterol, plasma phospholipid was somewhat higher in the high ratio group. Comparing mean values, ester cholesterol was 28 per cent lower and phospholipid 37 per cent higher in the high than in the normal ratio group of preeclampsia. In no case was the range of values in one group beyond the

range in the other as calculated from the means and standard deviations. Practically all the plasma lipid values in both groups of preeclampsia were higher than those previously found in normal pregnancy,³ but the differences were in no case sufficiently great to extend the expected range beyond that of normal gravidas. It may be concluded that this group of the toxemias of pregnancy tends to exhibit a slightly greater lipemia than normal pregnancy, but this is of academic interest only since cases even of eclampsia may show relatively low plasma lipid values.¹ From the practical point of view, one cannot distinguish preeclampsia from normal pregnancy by comparing plasma lipid values in any one given case.

On the other hand there is evident a significant difference in the phospholipid to cholesterol ratios. In the normal ratio group of preeclampsia, the mean value of the plasma P/TC ratio was 1.14 with a standard deviation of 0.17. This mean plus the standard deviation in this group ($= 1.31$) was thus lower than the mean minus the standard deviation of the high ratio group ($1.68 - 0.26 = 1.42$). Statistically, approximately 75 per cent of cases of the high ratio group may be expected to have plasma P/TC ratios above 75 per cent cases in the low or normal ratio group. Practically, this would appear to be a ready means of distinguishing between these two types of preeclampsia. On reviewing the case histories in relation to the subdivision of preeclampsia by means of the plasma P/TC ratios, it was found impossible to designate any further symptomatic difference between the types. In general the high ratio group showed more severe symptoms, but this was far from an absolute rule. In view of the similarity in findings between the high ratio group of preeclampsia and eclampsia itself,¹ it is offered that the two conditions represent one and the same disease, in the one case without and in the other case with convulsions. On the other hand, the majority of cases now included under the diagnosis of preeclampsia do not appear to be literally preeclamptic at all. Of the present series, 38 cases out of 49 were of a normal ratio (? noneclamptic) type or 78 per cent of the whole group. Since many milder cases diagnosed as preeclampsia were not included in this study, it is likely that the incidence of high ratio cases (? truly preeclamptic) would be not more than 10 per cent of the whole group.

Plasma cholesterol is composed of two fractions, a free or unbound type and cholesterol linked with fatty acids to form cholesterol esters. This latter fraction is usually designated ester cholesterol. In the plasma of normal persons, cholesterol esters constitute by weight the lipid of greatest bulk present. The question arose as to whether only the ratio of phospholipid to total cholesterol (P/TC) was the significant difference or if there were also significance differences in the ratio of phospholipid to free (P/FC) and to ester cholesterol (P/EC). Hence these latter

two ratios were also calculated and a statistical analysis of the results included in Table I. It may be seen that the P/FC ratio was higher in the high ratio group but that the ranges overlapped. However, a real difference existed in the P/EC ratios: the mean plus the standard deviation of the normal ratio group ($1.65 + 0.12 = 1.77$) was lower than the mean minus the standard deviation of the high ratio group ($2.73 - 0.74 = 1.99$). In fact the differences were of the same order of magnitude as those of the P/TC ratio. There would thus appear to be some disturbance in the normal balance between plasma phospholipid and plasma cholesterol esters in this group of preeclampsia, and it may be noted at this point that these two lipids constitute the bulk of all lipids normally present in human blood plasma. The, let us say, truly preeclamptic group may thus be distinguished from the remaining cases of preeclampsia by the plasma P/EC ratio as well as the plasma P/TC ratio. As a matter of fact it is easier to determine total cholesterol than ester cholesterol by the author's technic and by most other methods of lipid analysis. So that there is little to be gained and more work involved in determining the P/EC ratio rather than the P/TC ratio.

The significance of the phospholipid to cholesterol ratios is further evidenced by a comparison of their relative variation with that of the actual lipids. This has been shown in Table I under "standard deviation in percent of mean." It may be seen that in practically all cases there was less relative variation in the lipid ratios than in the actual lipid values. This would indicate that whereas the lipids themselves may vary considerably in value, there is a tendency toward the maintenance of a relatively constant ratio between them.

The lipid composition of the red blood cells in the two groups of preeclampsia has been given in Table II. In general, it may be said that the red cells of the normal ratio group contained slightly more of almost all lipids than was found in the red cells of normal gravidas,³ while those of the high ratio group contained slightly less than healthy pregnant women. This may be seen only in the means and is not apparent from individual cases, nor is the range of one group beyond the range of the other. From the first few cases studied, it was calculated that there was a significant increase in red cell neutral fat in the noneconvulsive toxemias,⁹ but further studies indicated, as herein pointed out, that this difference was not as great as was at first thought.

The relative variations of the red cell lipids are well illustrated in Table II. Neutral fat and cholesterol esters were found to be extremely variable and usually present in small quantities only. These red cell extracts were prepared in the conventional manner by heating for a short time the alcohol-ether extract of the hemolyzed cells. This procedure introduced colored decomposition products of hemoglobin, and from work now in progress, it is apparent that this colored matter tends

to give false high values for all lipids and especially neutral fat. However the same method of extraction was used in the eclamptic cases and a comparable one in normal pregnancy with both of which the present values have been compared. The lipids least variable in amount in the red cells were phospholipid and cholesterol, and these together constitute the bulk of red cell lipids.

TABLE II. AN ANALYSIS OF LIPID VALUES FOUND IN THE RED BLOOD CELLS IN PRE-ECLAMPSIA; THE RESULTS ARE EXPRESSED IN MG. PER 100 C.C. OF RED CELLS

VALUE	TOTAL LIPID	COMPOSITION OF TOTAL LIPID					
		NEU- TRAL FAT	TOTAL FATTY ACIDS	CHOLESTEROL			PHOS- PHO- LIPID
				TOTAL	ESTER	FREE	
<i>Normal Ratio Group</i>							
Minimum							
Total lipid	418	169	289	60	0	60	191
Maximum							
Total lipid	1067	377	732	128	0	128	562
Mean values	626	103	362	135	20	115	374
Standard deviation	177	142	142	35	31	34	95
Standard deviation in per cent of mean	28%	138%	39%	26%	155%	30%	26%
<i>High Ratio Group</i>							
Minimum							
Total lipid	236	0	112	69	0	69	167
Maximum							
Total lipid	805	311	540	127	0	127	367
Mean values	519	77	299	118	29	89	310
Standard deviation	181	118	139	37	37	26	74
Standard deviation in per cent of mean	35%	153%	47%	31%	128%	29%	24%

DISCUSSION

It has been shown that plotting the frequency distribution of plasma P/TC ratios in preeclampsia reveals the presence of two types of cases, one with a normal range of ratio values and a smaller group with elevated ratios. The findings in the latter group were comparable to those previously found in eclampsia. Hence, it is postulated that the high ratio group of preeclampsia represents cases of eclampsia without convulsions, while the normal ratio group may be an entirely separate condition. It cannot be gainsaid on present information that cases with a normal ratio may not go on to a high ratio if left untreated, and this point is being further investigated. From the small amount of data now available, it does not appear that a normal ratio commonly, if at all, becomes an increased one.

A statistical comparison of plasma and red cell lipids revealed that no lipid value possessed a range, determined from the mean plus and minus the standard deviation, significantly different in one group from the range in the other. The high ratio group of preeclampsia tended to have a slightly greater plasma lipid content and slightly lower red cell lipid

content on the average. The high ratio in this group was due chiefly to relatively higher values for phospholipid and lower values for ester cholesterol.

These several observations indicate some disturbance in lipid metabolism. It has been known for many years that lipid metabolism is altered in pregnancy, and the present work has shown that there occurs a further abnormal change in eclampsia and in a group which may be separated from what we now diagnose as preeclampsia. The nature of this disturbance in lipid metabolism has been, and still is, enveloped in obscurity; its cause, its importance, its effect, even its nature are largely unknown. In the past few years the author has been interested in these problems, but in spite of a good deal of work barely more than the surface has been scratched. It has been shown that the lipemia of pregnancy in women is analogous chemically to lipemias in other conditions and is characterized by an orderly increase in plasma lipid values with no change in the lipids of the red blood cells.³ Following parturition, the lipemia gradually subsides, but if normal lactation be prevented, a further lipemia supervenes which may be taken to indicate that the drying up of the breasts, though frequently resorted to, is in reality pathologic.¹⁰ At the end of pregnancy, the leucocyte count is usually elevated, but the lipid content of the white cells is not significantly changed: after labor there is an increase in the phospholipid and free cholesterol of the blood leucocytes (indicative of increased activity) and an increase in neutral fat which latter probably represents a scavenger action on the part of the white cells in removing debris fat from the involuting uterus.¹¹

Evidence has been presented that the human placenta is "permeable" to lipids and that a good deal of fatty substances, especially phospholipids, is absorbed by the human fetus from the umbilical circulation, suggesting that one result of the lipemia in the mother may possibly be the nourishment of the infant in utero.¹² The latter part of pregnancy in rabbits¹³ and guinea pigs¹⁴ was found associated with evidence of increased lipid metabolism in the placenta, suggesting that the placental tissues may be actively engaged in the transfer of lipids from the mother to the offspring. In the rabbit it was found that a marked increase in the lipid content of the fetus does not occur until the latter third or so of gestation,¹³ at which time the lipid metabolism of the placenta also increases.

It does not appear that the lipemia of pregnancy in women is of toxic origin, since an even greater lipemia may occur in the lower animals, for example guinea pigs.¹⁵ There is a certain amount of direct evidence that the changes in endocrine balance during pregnancy may have something to do with the changes in the concentration of blood lipids. By comparing blood lipid values in pregnant and pseudopregnant rabbits, it was possible to show that in early gestation certain

changes may be due to the direct or indirect effects of the products of conception and other changes to the direct or indirect effects of the presence of the corpus luteum.¹⁶ In the rabbit, in which a lipopenia or decrease in blood lipid values occurs during pregnancy (for the use of the term lipopenia see Boyd¹⁷), there is a marked rise and fall in the lipid composition of the ovary.¹⁸ On the other hand a lipemia is found during pregnancy in guinea pigs as in women¹⁵ and practically no change occurs in the lipid content of guinea pig ovaries throughout gestation.¹⁹ The author has also found in unpublished experiments the phospholipid and free cholesterol content of the human ovary to be quite low at the end of pregnancy in one or two cases studied. This evidence points to the endocrine system as a factor in the disturbed lipid metabolism of pregnancy but is far from sufficient to establish the exact relationship.

SUMMARY

The lipid composition of blood plasma and of the red blood cells was determined by oxidative micromethods in 49 cases of preeclampsia.

On the basis of the plasma P/TC ratio it was possible to show that these cases could be divided into two groups, one with a normal P/TC ratio and one in which the ratio was elevated as in eclampsia.

Cases with a high plasma P/TC ratio tended to have slightly higher plasma lipid values and slightly lower red cell lipid values than cases of a normal ratio.

The increase in the plasma P/TC ratio was due chiefly to relatively high plasma phospholipid and relatively low plasma ester cholesterol values.

It is offered that cases of preeclampsia with a high ratio are in reality eclampsia without convulsions, while the remaining normal ratio cases are not literally preeclamptic at all.

The significance of changes in lipid metabolism during gestation has been discussed.

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THERAPEUTIC ABORTION BY MEANS OF X-RAY*

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TEN years ago the Gynecological Service and the Radiotherapy Department of Mt. Sinai Hospital attempted a preliminary series of therapeutic abortions by means of x-ray. This was stimulated by the favorable report of Ganzoni and Widmer in 1925. The results obtained were sufficiently satisfactory to warrant a continuation of the method. We wish to report the results of our experience of ten years with the records of 200 fully studied consecutive cases.

The necessity for therapeutic abortion has been diminished somewhat in recent years. In part, this is due to a more general knowledge of contraception and, in part, to the more definite attention given this vital prophylactic service by physicians. There still occur too many pregnancies that should, perhaps, have been avoided. We attribute to our systematic campaign in bringing this to the attention of our hospital staff, the fact that we have a relatively small number of therapeutic abortions, of which those by x-ray outnumber other methods. It should be noted, as well, that many of these patients were not seen in our wards or out-patient departments prior to their pregnancy.

In the search for a surgically ideal method which would eliminate the mortality and morbidity of therapeutically indicated abortion, roentgen rays were thought of long ago. Experiments in the interruption of pregnancy were made before 1907 (M. Fraenkel), but the early reports must be discounted because of the unreliability and uncertainty of the dosage. It is only since the era of accurate dosage measurement and improved x-ray apparatus, that we can estimate the results.

Routinely, when the question of interruption arises, a consultation is held between the representatives of the gynecologic, the radiotherapy department and the department in charge of the indicating condition. At this consultation, both the question of intervention and the method are decided. The patient, is, of course, informed of the possibility of a permanent amenorrhea, and written consent is obtained. Our indications have been medical only, not economic or eugenic. Multiparity plays a rôle only when the existence of a sufficiently large family makes it unfair to ask the patient to assume an extraordinary risk for the sake of progeny.

*Read at a meeting of the New York Obstetrical Society, May 12, 1936.

After radiation has been decided upon, the patient is prepared, an enema is given, and the pelvis is rayed by means of the teechnie which will be described later on. When the treatment is completed, the woman is instructed to return at weekly intervals and/or at the first sign of bleeding or cramps. These usually occur about three to four weeks after treatment, and the patient is then admitted to the hospital. Ordinarily, she spontaneously aborts, expelling a dead fetus, most often enclosed in an intact sac. Usually there is only slight bleeding compared with that seen in an ordinary miscarriage. The convalescence is quite uniformly uneventful and the patient is in a condition to be discharged from the hospital in a few days, though she is usually kept somewhat longer.

Instruction is given to avoid intercourse in the interval between treatment and abortion. One woman who failed to do this and contracted gonorrhea, ran a postoperative febrile course as a result of pelvic infection in sharp contrast to the uniformly uneventful convalescence of the others.

Upon discharge, patients are referred to our follow-up, also to the contraceptive clinic for advice to be followed, even though they are amenorrheic. Occasionally, due either to lack of cooperation or (far less likely) to failure of contraception, a second pregnancy results. The treatment can then be repeated. We have seven successful repetitions of the treatment, all of these patients remaining amenorrheic to date.

In some cases, the sac ruptures and the fetus and placenta are expelled attached to each other. Much less often the placenta is retained for a brief time. The subsequent involution is quite uniformly satisfactory. Retention of fragments does not follow as it does so frequently when a live fetus is surgically removed.

In the event of premonitory bleeding, when examination shows a gaping cervix, we have frequently administered small doses of pituitrin which expedite the completion of the delivery. It is probable that slight staining, especially with a closed cervix, should be treated with a dose of "patience." If, however, examination reveals an ovum stuck in a *dilated* cervical canal, a simple twist of a forceps suffices to terminate the whole process. This requires no anesthesia and should not be classified as an operation.

We believe that the abortion is caused by the death of the fetus as a direct result of the radiation, rather than through any effect on the ovaries or the placenta. Since young growing cells have a greater sensitivity to x-ray than older ones, one can destroy the fetus without any considerable damage to the uterine musculature and the parametrial tissues. The entire lymphatic apparatus is the most sensitive of the tissues. On the other hand, Momigliano, in his work on irradiated rabbits, seems to have shown definite changes in the placenta, shutting off fetal nutrition. We have not been able to find unequivocal changes in the placenta in our cases.

These cases are, in reality, excellent examples of missed abortions. We know that the fetus dies sometime before the expulsion of the uterine contents (usually fourteen days after treatment), and cannot be differentiated from the morphologic picture of missed abortion. The fetus is flattened, loses its typical translucency, the vessels cannot be seen through the skin, which is macerated, the amniotic fluid is dark brown and turbid as in missed abortion, expulsion is preceded by a stage of spotting and the discharge of thin fluid, followed by cramps.

According to Von Graefe, the retention in the uterus of the dead products may be related to a decreased irritability of the uterus. Tausig agrees that the gradual death of the fetus permits an adaptation so that it does not act as a foreign body so promptly. What does eventually initiate the uterine contractions is not definitely known, though doubtless the answer will be forthcoming as a result of our rapidly increasing knowledge of the interplay of the internal secretions.

METHOD

The technic used throughout this series of cases was uniform. Sixty per cent of a skin erythema dose (600 r. measured in air is considered an erythema dose) was given to the center of the uterus. Calculation of the amount that had to be given to the skin to obtain this dose was determined by making outlines of the pelvis and estimating the quantity necessary to obtain the desired dose in the uterus according to the methods of Holfelder and Weatherwax. In the average case with an anteroposterior pelvic diameter of 20 cm., two opposing fields each receiving 600 r. in air will suffice if the apparatus will deliver 35 per cent S.F.D. at 10 cm. depth. When the anteroposterior diameter is larger than 20 cm., compression cones or strapping of a pendulous abdomen will aid in reducing the distance to the uterus. When adequate reduction of the distance is not possible, additional portals of entry (three to six) may be required.

The apparatus should be calibrated by a competent physicist and if possible a constant reading dosimeter between the tube and the patient will aid in giving the correct dosage. The physical factors are 180-200 K.V., 50 cm. F.S.D., filter 0.5 mm. copper 1 mm. aluminum, size of portals average 15 x 20 cm. (suprapubic and sacral including the adnexa). The treatment should be given on two or three successive days.

A mild cathartic is given on the evening before treatment and the bladder is always emptied immediately before treatment is administered. The outline of the uterus is mapped out on the anterior abdominal wall with a colored pencil and the central beam is directed through the middle of the fundus.

When there is a discrepancy between the length of amenorrhea and the size of the uterus, we advise a radiograph of the pelvis to determine if possible the size of the fetus. The presence of fibroids is not a contra-indication to treatment.

It is most important to keep certain facts in mind in the case management after radiation. Since the time interval varies so, we must be very patient, and if convinced that the embryo is not growing, be content to wait. No harm can result. Febrile and toxic symptoms do not develop.

The checks on viability are the absence of growth (controlled by weekly examinations), the Aschheim-Zondek or Friedman test, which may, however, remain positive for some weeks, and the test for female sex hormone which becomes negative even when the Aschheim-Zondek test remains positive.

If continued growth, etc., convince us that the fetus is still alive after four weeks, radiation may be repeated, provided that the size of the uterus at that time is not larger than that of a four months' pregnancy. There are several instances in this series in which this procedure was carried out successfully.

The pregnancy must never be permitted to continue to term, following x-ray treatment, because of the definite possibility of the birth of an abnormal child.

Wintz believes that 50 per cent of children who have received such large antenatal radiation will be pathologic. Goldstein and Wechsler have demonstrated definite eye changes in the form of typical rosettes of infiltrating cells in the retina, etc., in our material.

The possible effect on subsequent pregnancies is undecided and seems far more doubtful. We know of five such pregnancies and, so far, the children have seemed perfectly normal. E. Maurer reports fourteen children of irradiated mothers, none of whom were abnormal. He concludes from the literature that one cannot speak for or against the safety of conceiving after radiation. Of 229 such children, 25 per cent showed some pathologic findings, but critical sifting reduces this to a very small number in which one could possibly attribute the defect to the radiation. In 1931, the German Society for Heredity issued a warning of possible injury to the germ cell which might become manifested only after a number of generations.

We agree that it should be made clear to candidates for this treatment that they should not plan to have more children, and the treatment should be restricted to patients who are willing to cooperate fully in this respect, and in whom the indications are permanent and absolute.

CASE REPORTS

We are reporting 200 fully studied cases. Of these patients, all but 8 aborted dead fetuses. That would give a 96 per cent success. However, of these there were 12, or 6 per cent, in whom the sac or the

placenta was removed from the cervix or uterus without anesthesia. If we exclude these cases as partial failures from the standpoint of a perfect method, we have been 90 per cent successful.

The ages of the patients varied from sixteen to forty-eight, the average being thirty-two. The parity varied from no children to 14, with an average number of 3 children to a woman. Many had had previous surgical abortions, often with stormy convalescences. Twenty-two, or 11 per cent, aborted at home (with

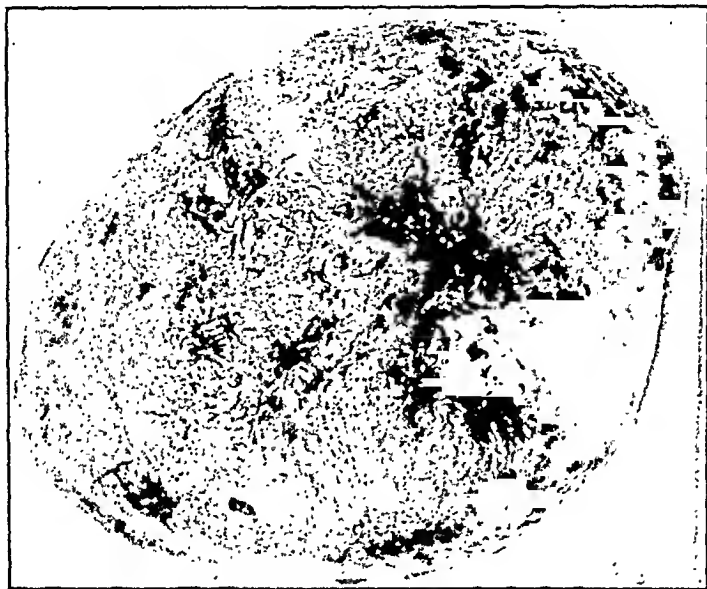


Fig. 1.—Illustrating the fetus and placenta expelled in an intact sac, following roentgen treatment.



Fig. 2.—Illustrating fetus and placenta expelled after rupture of the sac. The fetuses are in varying stages of flattening and maceration.

so few symptoms that they did not think it necessary to come to the hospital). The average hospital stay of the others was nine days. This would be misleading if we did not remember that we are dealing with a debilitated group, the longer hospital stay necessitated by the general medical condition which was the indication for intervention.

The interval between treatment and abortion varied from three days to one hundred and fifty, the majority, 60 per cent, occurring between the nineteenth

and thirty-fifth days. The average was thirty-three days. The occasional very rapid or very long delayed abortions are quite exceptional. We are sure that many of the reported failures, including some of our own earlier cases, were mistakes in judgment and instances of needless interference as evidenced by the findings. The amount of bleeding was usually slight. In 12, it was moderate, in 5 profuse, but always easily controlled. The period of amenorrhea afterward was very variable. In general, it can be stated that almost all of the patients below the age of twenty-five will have a return of menstruation though the amenorrhea may vary from one to forty-eight months. In the patients from twenty-five to thirty, one-half have remained amenorrheic so far. Of those who were thirty to thirty-five, slightly more than half. In the age group thirty-five to forty, about two-thirds, and those over forty, all became amenorrheic. In no case can we promise that menstruation will surely return. The majority of the patients had some menopausal symptoms. These are not easy to evaluate. According to the records of our follow-up, they were, in most instances, mild. Wintz calls attention to the milder menopause in women rayed during the period of amenorrhea, and feels that this is related to the fact that the endocrine system is, in a sense, adapted to amenorrhea and adjusts itself more easily. Certainly the complaints of our patients on this score were in no way a major problem in this series.

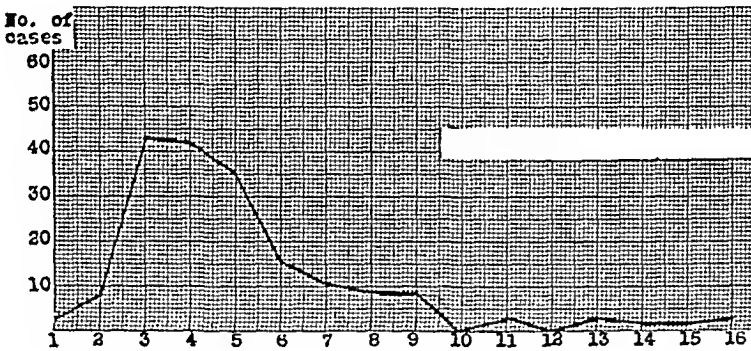


Chart 1.—Graph showing interval in weeks between application of roentgen therapy and the subsequent abortion in 200 successive cases.

The patients have been followed, in most instances, for many years. Unfortunately, with a shifting population, this has not always been possible. Ideally, it is most important, as we noted return of menstruation with subsequent pregnancy as long as fifty-four months after treatment. (In this interesting case, a vesicovaginal fistula had been cured in the meantime, and the patient so extraordinarily improved in health that it was possible for her to go through a normal pregnancy. She delivered an apparently healthy child.) No patients died from the treatment. Several women in this series have died of the associated medical lesion or some intercurrent condition, some time afterward.

TABLE I

Number of cases—200	
Failures	8 - 4%
Requiring removal with forceps—without anesthesia	12 - 6%
Completely successful	90%
Clinically successful	96%
Died—none	
Morbidity	
Fever	2 - 1%
Sharp bleeding	4 - 2%
Repetition of pregnancy	8 - 4%
Repetition of treatment	7 - 3.5%

The abortions were performed for the following indications: A. *Very frequent*: Chronic cardiac valvular disease, 74 cases; pulmonary tuberculosis, 27 cases; and Graves' disease, 19 cases. These three lesions represent two-thirds of all the cases.

B. *Not infrequent*: Postoperative (especially following recent operations for large central hernias or tuberculous kidney), 16 cases; nephritis, 12 cases; and malignant psychoneurosis, 9 cases.

C. *Occasional indications*: Mental deficiency, 4 cases; malignant hypertension, 4 cases; severe diabetes, 4 cases; surgical tuberculosis, 4 cases; and asthma, 4 cases.

D. *Among rare indications are included*: Arthritis with ankylosis, 2 cases; congenital cardiac disease, 2 cases; pelvic cellulitis, 2 cases; Hodgkin's disease, 1 case; Banti's disease, 1 case; retinitis proliferans, 1 case; ulcerative colitis, 1 case; spinal cord tumor, 1 case; glioma, 1 case; and extreme malnutrition, 1 case.

We have been particularly interested in the psychologic effect of this whole procedure. Some authors have emphasized the mental strain involved in asking these women to wait over an extended period of time for the completion of the abortion. Some have been concerned with the question of the loss of libido. Our own observations have led us to believe that in this type of patient suffering from some severe organic disease, the mental attitude after x-ray abortion is not bad, if we have prepared the patient by preliminary instruction and reassurance. A very few have complained of diminution of libido and loss of orgasm. This is just as likely to be psychogenic in origin and would not be unexpected in any series of 200 women followed for a period of time. In the cases of malignant psychoneurosis, we are dealing with women in whom we cannot evaluate loss of libido or orgasm so simply. A most careful estimate of the personality of the patients in this group and the possible traumatic effect is imperative for obvious reasons.

If one could shorten the period between death of the fetus and expulsion, it might be an improvement in the method. Wintz feels that the inclusion of the ovaries in the irradiated field is vital, to eliminate the possibility of preserving a glandular function of the ovary which might inhibit expulsion.

The failures may be classified into two groups: (1) complete failures and (2) clinical failures. A complete failure refers to the cases in which the fetus was not dead and continued to grow. Clinical failure refers to those cases in which the fetus was killed but where there was retention of a portion of the products of conception, usually a fragment of placenta in the gaping cervix.

Of the 8 failures enumerated in Table II, Case 1 should be classified as a clinical failure. Although the patient in Case 4 felt life before treatment was instituted, the roentgen method was tried because of the severity of the patient's cardiac condition. A dead fetus was expelled shortly after the introduction of a Voorhees' bag, and it is quite likely that the fetus would have been expelled spontaneously had we waited. The same is true in Cases 3 and 8. Review of the treatment in Case 5 showed definite undertreatment. No definite reason for failure could be found in the remaining 3 cases other than possible faulty technique.

The advantages of the method include the absence of morbidity in patients in whom an anesthesia is dangerous, especially the cardiac, tuberculous, and nephritic patients; the absence of any mortality, in respect to which this method is incomparably superior; the absence of infection, since there is no introduction of a foreign body into the uterus; the minimal bleeding due to the mummification of the fetus and closure of the blood sinuses; the avoidance of retention of products of conception and the period of amenorrhea which seems to be of some value in cases of pulmonary tuberculosis. It might be interesting to compare 200 hospital cases of therapeutic abortion reported by P. Kühnel. These were done by skilled operators. There were 2 operative deaths, severe hemorrhage in 16, infections in 36, tears of the cervix in 18, and "accidents" in 22, including 2 perforations of the uterus.

The disadvantages should be carefully considered: The method may fail. Then we are confronted with the necessity of performing a surgical abortion at a somewhat later time. Then there is the possibility that a patient will insist on a subsequent pregnancy and delivery, and although we have not as yet seen any deleterious effects on later children, the subject has not been studied for a sufficiently long time for any categorical statement. Then there is the question of the menopause symptoms which may persist for years, and the loss of libido complained of in a few cases.

The disadvantages must be weighed in every individual case against the disadvantages of either a curettage or a hysterotomy. It should be superfluous for me to warn against the wholesale application of such a method. In early pregnancy in

TABLE II. FAILURES IN 200 CASES OF ROENTGEN THERAPEUTIC ABORTION

NAME	AGE	ADMISSION	GRAVID— WK.	TREAT- MENT	RESULT
1 G. W. (Tbc.)	32	4/30/26	8	5/ 1/26 5/ 2/26	5/23/26 Placenta removed from cervix
2 R. R. (s. c. tumor)	31	2/18/36	12-14	2/19/26 2/20/26	Bag introduced 4/17/26
3 E. S. (C. C. V. D.)	36	3/18/27	12	3/22/27 3/23/27	4/19/27 Hysterotomy
4 L. K. (C. C. V. D.)	37	10/ 2/29	8 Felt life	10/ 2/29 10/ 3/20	11/7/19
5 L. R. (C. C. V. D.)	25	6/22/29	8	6/24/29 6/25/29 (Under- treated)	11/11/29 Bag introduced
6 L. G. (Tbc.)	30	7/11/31	8	7/ 8/31 7/ 9/31	Spotted cramps 8/12/31 Hysterectomy 11/19/31
7 A. H. (C. C. V. D.)	25	3/ 5/30	12	9/ 9/30 9/10/30	1/3/31 Bougie intro- duced
8 M. R. (asthma)	25	12/25/32	8	12/28/32 12/20/32	2/27/33 Hysterotomy

a debilitated patient with an acute exacerbation of a chronic disease, especially tuberculosis or severe cardiac disease, when subsequent pregnancies are absolutely interdicted, it seems ideal. Now and then it offers a way out when one's hands are otherwise tied. Although the total percentage of patients in whom this method can or should be used may be small, if we consider that 60,000 to 80,000 therapeutic abortions are performed annually with a heavy toll in mortality and morbidity (Tauszig), there would seem to be an actually large number of women who could be saved by this method.

SUMMARY

We are reporting ten years of experience with therapeutic abortions by x-ray.

We have had 200 ward patients with a clinical success in 96 per cent and an ideal success in 90 per cent.

The method is recommended for pregnancies of not more than fourteen weeks' duration, in women who are suffering from a serious lesion

which would make surgical interruption very dangerous and who should not again become pregnant. This is particularly valid for women over thirty-five years of age.

The method has no mortality and remarkably low morbidity, but it does require the closest cooperation between clinician, radiotherapist, and gynecologist, as well as scrupulous observation, control, and follow-up of the patient.

If the treatment should fail, under no circumstances should the pregnancy be permitted to continue.

Irrespective of amenorrhea, patients should receive contraceptive instruction after the abortion.

The clinical picture is that of a missed abortion with a latent interval averaging about four and one-half weeks.

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DISCUSSION

DR. SEYMOUR WIMPFHEIMER.—Usually the menopausal symptoms after this x-ray method do not seem to affect the patient's condition adversely, and I have followed the blood pressures in several cases over a number of years and found very little change. I have carried out this method in eleven cases at Montefiore Hospital. Six of the patients were seriously ill with pulmonary tuberculosis, four were suffering from cardiac disease, two of whom were in cardiac failure. We were successful in all our cases. The method and the results in the main coincided with those given by Mayer and Harris.

DR. IRA I. KAPLAN.—We have tried altogether 8 cases at Bellevue Hospital in the course of the past ten years. We have not used the x-ray method of producing abortion more frequently, because we have not been successful. The description of the technic as given by Harris shows me that our technic was entirely different. Yet we have been successful in sterilizing a great many patients, and it is hard for me to realize just now why our abortion results were so unsuccessful.

The first case that we tried was a woman thirty-six years of age who two years previously had had a surgical abortion and x-ray sterilization because of recurrent carcinoma of the breast. For a year she had remained amenorrheic but in October, 1925, reported to us that she was pregnant. We gave her an intensive course of

x-ray therapy and waited seventeen days, but no abortion occurred. She was then referred to Dr. Holden who did a hysterotomy and found twins. The specimens were sent to Streeter of the Department of Embryology of the Carnegie Institute, who reported as follows: "The tissues in both the chorion and the embryo are greatly macerated, indicating that death had occurred a long time before abortion. We assume the period of development to be 10 $\frac{1}{4}$ weeks."

The second case had a marked pulmonary tuberculosis, a gravida iv, para i and at the time we were asked to see her was pregnant two or three months. She received x-ray therapy, and we waited six weeks. No abortion occurring, hysterotomy was done in April, 1927, and a macerated fetus was removed. In January, 1928, after almost nine months of complete amenorrhea, she reported to us with definite signs of pregnancy. The question arose as to whether we should abort her on account of the previous x-ray sterilization, but she was permitted to go to term and was delivered of a perfectly normal baby. This child is now 8 years old and perfectly normal. The mother has no evidence of active tuberculosis and has menstruated normally since her last delivery.

Our third case was that of a colored woman, twenty-one years of age, para i, whom we saw in March, 1927. She had active pulmonary tuberculosis and her previous pregnancy had ended only four months previously. She was first treated by pneumothorax to control the tuberculosis and was then given x-ray therapy when about two and a half months pregnant. We waited five weeks and she suddenly aborted. That was the first successful result we had had.

The fourth patient, seen in December, 1927, was a little hunchback with marked anemia, who had been pregnant ten times previously and had had three miscarriages. She had seven living children. We gave her x-ray when the pregnancy was at three months and waited seven weeks, but nothing occurred and hysterotomy was then performed. I will read to you later Dr. Streeter's report of this case and the next one.

The fifth patient, seen in January, 1928, was a white woman, thirty-seven years old, gravida ix, with very severe tuberculosis. She was given x-ray therapy when two months pregnant, but after seven weeks, nothing having happened, hysterotomy was performed.

The fetuses from the two previous cases were sent to Dr. Streeter. He wrote that the baby of the first case appeared to be normal, nineteen to twenty weeks of age. The other, Streeter said, was ten weeks old. He believed that these fetuses must have been living up to the time of abortion. "After the pregnancy has started and has developed past one month," Dr. Streeter says, "it is too late to damage the fetus without damaging at the same time the mother." His subsequent report on these fetuses, after sectioning, was that there was no damage to the tissues.

The sixth case was one of carcinoma of the cervix. The patient came to us about two months pregnant. She was given x-ray therapy, but no abortion occurred. She continued to term and had a normal child, delivered through the carcinomatous cervix. The child was found to be perfectly normal at the time of delivery in May, 1929, at another hospital. The mother was well for a time after radium treatment of the carcinoma of the cervix.

In July, 1933, the seventh case, a woman with severe tuberculosis and a cardiac condition, gravida ii, two months pregnant, was treated by x-ray therapy. She spontaneously aborted after seven weeks. One month after this she was operated upon in the Bellevue Hospital for acute peritonitis which it was proved followed the perforation of a tuberculous tube.

On Jan. 5, 1934, we accepted the eighth patient, whose diagnosis was pulmonary tuberculosis with pneumothorax and gynecologic tuberculosis. She was a gravida i,

para 0, now two months pregnant, although the Aschheim-Zondek test was reported negative. Six weeks after treatment, no abortion having taken place, she was operated upon and a living four-and-one-half-month-old fetus removed.

Thus of 8 patients treated, only two have been successful. We conclude therefore that radiation given during pregnancy is not always followed by abortion. Radiation so given is usually fatal to the very young fetus, but normal children may be born. Nevertheless if the woman does not abort, we think that surgical abortion should be performed.

DR. WILLIAM E. STUDDIFORD.—I would like to say a word or two in defense of operative therapeutic abortion.

There are not many conditions in which one cannot perform an operative abortion if there is a skillful anesthetist at hand. There are no failures, and if therapeutic abortion is properly done—and that means the complete removal of the ovum—there should be no hemorrhage. The incidence of infection is not great.

One of the city medical examiners told me the other day that he had never had a case of therapeutic abortion come to his attention at autopsy as a medical examiner's case.

DR. HENRY T. BURNS.—There are very few cases where there is a contraindication to operation and, as far as anesthesia is concerned, I have done 8 or 9 therapeutic abortions under a local, using novocaine, which works very nicely and with very little discomfort. We use one-half of 1 per cent novocaine solution along the base of the broad ligament and also under the bladder fold and wait about five minutes for the novocaine to take effect. The best results follow in women who have never borne children, because there is no scar tissue about the cervix to interfere with infiltration of the novocaine.

DR. NELSON B. SACKETT.—I would like to report the case of one patient admitted to Woman's Hospital when three and one-half months pregnant with carcinoma of the cervix involving the entire portio vaginalis. We gave her the usual dose of radium to the cervix, assuming that abortion would follow soon afterward. During the next three weeks, with the Aschheim-Zondek test persistently positive, the patient had a few vague pains, stained a few times but did not abort. We decided then to employ roentgen therapy, and she was given 800 r. units through each of four portals in eight days. Despite all that treatment she still failed to abort, although the Aschheim-Zondek test now became negative. The carcinoma had shown virtually no regression under this treatment, and eventually the patient came to Wertheim hysterectomy after which she died.

I merely mention this experience as an example of the type of case where a great deal of irradiation by x-rays and radium fails to produce abortion, although we assume that the fetus was killed by the radiation. The hysterectomy specimen revealed a shriveled, complete ovum and an undilated cervix infiltrated with carcinoma.

DR. C. FREDERICK JELLINGHAUS.—I feel the indications mentioned by the speaker were rather broad. For example, some patients with Graves' disease can have their thyroid operated upon, the pregnancy being allowed to go to term. He stated an internist, a gynecologist, and a radiologist decided whether the abortion was indicated or not. I should suggest adding an obstetrician to aid in making the decision.

The speaker stated there is always a risk of amenorrhea after the x-ray treatment and that in patients between twenty-five and thirty years of age amenorrhea

followed in 50 per cent. I am mid-Victorian and believe in the old adage: "A woman's best friend is her menstruation," and for this reason I think in most cases the x-ray method of bringing on an abortion is wrong.

DR. WILLIAM H. CARY.—One point that Dr. Mayer's paper did not make perfectly clear to me concerns the most favorable time in pregnancy for the application of the irradiation. Assuming that a very early diagnosis is made, should some time necessarily pass before the irradiation? In all the cases reported the fetus and placenta were both definitely developed.

DR. FRANK R. SMITH.—I would like to ask the speakers just what they consider a sterilizing dose of x-ray. I have delivered patients who received 1,800 mg. hours of radium in the uterus and had become pregnant afterward. I have had one patient in fact who received 2,500 mc. hr. of radium in the cervix while pregnant, and went to term.

DR. MAX D. MAYER (closing).—In answer to Dr. Jellinghaus. I am willing to disclose the records of every one of these 200 cases to any member of the Society and believe that they will agree that not one of these patients should have been permitted to continue their pregnancy. I feel that an average of 20 therapeutic abortions annually for a hospital the size of Mount Sinai with a 750-bed capacity is not excessive.

Answering Dr. Cary's question about the time, I would say that there was always an interval between the diagnosis of pregnancy and the decision, which time was, in most cases, occupied in studying the patient.

DR. WILLIAM HARRIS (closing).—There were a number of cases in this group where the only alternatives were hysterotomy or roentgen therapy for the termination of the pregnancy. This was especially true in four cases with ankylosing arthritis of both hips where pelvic examination could be performed only with the patient absolutely flat, and where no operative procedure could be done by the vaginal route.

We have had surgical mortalities from therapeutic abortion. One patient refused the menopause that would follow roentgen abortion, and curettage resulted in an anesthetic death. We have done a few abortions with local anesthesia around the cervix, but the majority of these cases presented by Dr. Mayer were crippled patients who certainly would have had some morbidity if not mortality had surgical intervention been used.

I am afraid that Dr. Kaplan was using the phrase sterilizing effect of radiation rather loosely. Forty per cent of an erythema dose is enough to stop any patient from menstruating for a while; it will stop a patient over forty years of age completely. We should not use the word sterilizing, but instead should say the production of an amenorrhea by irradiation because you are not always sure of sterilization unless massive doses are given. We have had patients who became pregnant during the amenorrheic phase, several patients under thirty-five years of age, and one between thirty-five and forty.

One can definitely sterilize a patient even in the strict sense of the term. You render a patient amenorrheic so that she will not conceive again if you give three series of 40 per cent of an erythema dose each, or three times 240 r. to the ovaries within one year. Now the reason that a patient may menstruate after the insertion of a radium tube in a cancer of the cervix is because the radium tube is placed in the cervix and from this position one gets very little irradiation from the end of a radium tube into the fundus. When one gives 1,800 mg. hours in the endometrial cavity, the

main effect is on the endometrium with very little effect on the ovary. The amenorrhea produced is due chiefly to the secondary effect on the ovaries from destruction of the endometrium.

You do not get very much radiation effect at the end of a radium tube; you get it mainly at right angles to the tube. That explains why you can get menstruation, or why pregnancy will continue after a maximum dose for carcinoma of the cervix is given with a tube which does not extend beyond the internal os.

CALCIUM AND PHOSPHATASE STUDIES IN CANCER OF THE FEMALE SEX WITH A CONSIDERATION OF BASAL METABOLIC RATE AND URINE pH

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IN PREVIOUS reports we have shown that the apparent calcium deficiency shown by blood and, more particularly, blister fluid of patients with malignant disease is related to decreased protein content of the fluids. Because of recent interesting and contradicting reports of the relation of phosphatase to malignancy,³⁻⁷ we have continued our work with the addition of phosphatase values. On the same series of cases we have determinations of basal metabolic rate and urinary pH. The cancer group contains cases of gynecologic malignancy while our control series is taken from the same ward, but has no known malignancy.

METHODS

Collection of samples and determination of the various chemical constituents have been described in our previous paper.² Phosphatase values were determined by the King and Armstrong⁸ method. Preliminary experience with this method gave us difficulty with turbidity which was avoided by omitting the Li_2SO_4 from the phenol reagent. Private communication with Armstrong has confirmed the need of this modification in some cases, with no effect on the accuracy of the method. All samples were analyzed as soon as taken. This is especially important, since Bodansky⁹ has noted increase in phosphatase on standing. This change may be due to change in pH of the blood serum, according to Woodward and coworkers.⁶ Control determinations using thymol blue indicator for spot testing have shown that our substrate-serum mixture has a pH of 8.7 before and after digestion. The substrate after standing two months becomes slightly more alkaline and slightly higher values are obtained. This increase is of the order of 5 per cent with a substrate two months old, and since the substrate we used was always less than one month old and none of the serums would have abnormal pH, our results are not affected by pH change. The phosphatase values are for $\text{pH } 8.7 \pm 0.1$.

For basal metabolic rate determinations we are indebted to Mrs. Mildred Woodward here. The Benedict-Roth apparatus was used and corrections were applied for height, weight, and body temperature. Each case was run after sixteen hours' fasting, and each was a hospital patient brought to the laboratory while in bed. The average of two determinations is taken for the final reading.

Urinary pH determinations were run on a fasting morning specimen obtained by catheter and compared in a LaMotte indicator block within fifteen minutes after collection.

RESULTS

Table I gives the results obtained for 26 cases with no demonstrable malignancy. Twenty-four of these were diagnosed by surgical biopsy as fibroids, cervical polyps, hyperplastic endometrium, pelvic inflammation, and tuberculosis of the uterus. One was a case of cystocele and rectocele, and the other a case of vesicovaginal and rectovaginal fistulas following radium treatment for cancer of the cervix six years ago, who is now cancer free as proved by biopsy and laparotomy.

Table II gives the results on 50 cases of malignancy, each of which was diagnosed by biopsy.

Table III gives a summary of the minimum, maximum, and average values of each of the determinations.

DISCUSSION

Results for calcium, inorganic phosphorus and protein correspond with our former series of cases.² It is interesting to note that average protein and calcium values in both blood and blister fluid run slightly higher than the former series, and inorganic phosphorus values run slightly lower. This we attribute to seasonal difference. Most of the present series were run in the summer months when vitamin intake, sunlight, and balanced diet had more influence than on our former series of cases during the winter and spring.

This second set of cases affirms our former conclusion that there is no change in calcium and phosphorus metabolism in malignancy that is not related to changes in protein content of the body fluids as influenced by malnutrition, cachexia, or chronic loss of albumin.

The additional set of values for calcium ion concentrations, reported here, confirm our former finding that malignant disease does not affect the calcium ion concentration of blood serum (calculated according to McLean and Hastings¹⁰), and that in malignancy there is very likely no change in parathyroid function.

With the exception of Case 69 (Table I) and Cases 14, 26, 27, 33, 31, 36, 42 (Table II), the phosphatase values in both series of cases are within normal limits. The last three cases, 31, 36, and 42, are only slightly above the limit set by King and Armstrong and according to the work by Yaguda¹¹ may be within the normal for the method. Case 69 of our nonmalignant group with a phosphatase value of 21.6 units seems to show that occasionally the normal value may exceed 12 units, as we have no explanations for the raised value here. We have sought particularly evidence for Paget's disease^{11, 12} or liver damage^{11, 13} but found none. Cases 14 and 33 are patients with probable liver metastases, as this was considered a possibility by physical examination, and the appearance of the liver of Case 33 at operation was suggestive of cirrhosis or metastatic carcinoma with no visible tumors. Gutman et al.¹² have reported phosphatase increase in metastases to liver. For Cases 26 and 27 we have no explanation for the high phosphatase values. The patient in Case 26 is in good health one year after radium treatment. The patient in Case 27 died at home seven months after treatment. It is possible that bone or liver metastases may

TABLE I. RESULTS ON NONMALIGNANT CASES

CASE	DIAGNOSIS*	AGE	BLOOD					BILSTER FLUID					URINE pH	BMR
			Ca	P	Pr	pH	Ca++	Ca	P	Pr	pH	Ca++		
8	Cervical polyp	72	10.33	3.71	6.87	6.5	4.6	9.29	3.85	6.24	6.6	4.4	-	-
10	Pituitary	50	10.63	4.25	7.32	3.9	4.6	8.95	4.31	6.15	3.8	4.3	7.6	-
15	Hyper. endometrium	42	10.70	4.41	7.56	4.2	4.5	8.82	4.41	5.88	8.6	4.3	5.4	+16.0
17	Hyper. endomet., polyp	50	10.32	3.90	7.80	6.3	4.3	7.90	3.88	6.36	4.9	3.6	4.8	-12.7
18	Hyper. endomet., P. I. D.	22	10.44	4.27	7.68	4.2	4.4	9.20	4.40	6.36	3.6	4.3	5.8	-5.9
21	Hyper. endometrium	40	9.90	2.72	4.23	4.1	5.2	8.00	2.81	3.54	4.2	4.9	5.1	+6.0
22	Hyper. endometrium	39	9.80	2.43	6.30	4.7	4.6	8.73	2.69	4.90	6.5	4.6	5.4	+12.5
23	Hyper. endometrium	36	10.80	2.38	7.98	4.8	4.4	9.20	2.63	6.24	5.4	4.3	5.2	+9.0
24	Hyper. endometrium	37	10.00	2.78	7.62	9.8	4.2	8.98	3.03	6.24	10.8	4.2	5.3	+4.3
22	Retained secundines	50	9.80	2.64	5.88	5.9	4.8	8.43	2.78	4.98	3.9	4.5	5.2	-1.4
34	Fibroids	36	10.01	3.37	7.25	9.0	4.4	8.80	3.50	6.36	8.0	4.1	5.5	-5.6
35	Ov. cyst, atroph. endomet.	30	10.38	3.16	7.20	4.5	4.5	8.55	3.44	6.06	3.8	4.1	7.1	-6.8
37	Cervical polyp	46	10.75	3.97	6.99	6.8	4.8	9.30	4.41	6.06	4.8	4.5	5.4	-4.0
38	Chronic cervicitis	46	9.60	2.50	6.24	9.0	4.5	7.95	2.53	5.19	9.3	4.1	6.4	+1.0
40	Hyper. endomet., fibroid	49	10.00	3.44	6.03	12.5	4.8	8.65	3.66	4.74	9.6	4.7	6.1	+4.5
43	Hyper. endometrium	48	10.80	2.81	6.54	8.3	5.0	9.12	2.84	5.22	6.3	4.7	7.2	-3.6
48	Fibroids, arthritis	50	10.22	4.28	7.11	9.7	4.5	8.70	4.34	5.64	6.8	4.3	4.6	+9.5
53	Cervical polyps	50	10.30	3.06	7.44	7.2	4.4	8.55	3.80	5.64	5.6	4.2	6.4	+0.4
55	Cervical polyps	36	10.21	3.20	6.66	5.3	4.7	8.92	3.41	5.82	5.6	4.3	5.0	-4.3
61	Metrorrh., hypothyroid	16	10.05	3.18	6.96	8.8	4.5	8.75	3.38	5.40	8.6	4.5	5.3	-14.3
62	Inflammation vagina	62	10.38	3.96	7.62	7.5	4.4	9.00	4.10	6.18	5.4	4.3	6.2	+0.5
64	Hyper. endometrium	40	10.73	3.55	6.90	10.8	4.8	9.30	3.75	6.15	9.9	4.4	5.0	+30.0
68	Hyper. endometrium	41	10.16	3.25	6.30	10.1	4.8	8.28	3.31	4.80	9.6	4.4	7.1	-
69	P. B. of uterus	45	11.03	3.52	7.32	21.6	4.8	8.69	3.44	6.45	20.2	4.0	7.4	+10.8
74	Hyperplasia, fibroids	49	10.20	3.73	8.10	6.0	4.2	8.68	3.69	6.15	4.5	4.2	7.2	+12.0
75	Cysto- and rectocele	54	10.50	4.04	7.98	5.6	4.3	8.98	4.41	6.00	3.9	4.3	7.2	-1.3
Average		45.7	10.27	3.40	6.99	7.52	4.57	8.77	3.58	5.77	6.94	4.33	5.73	+2.5

*Calcium (Ca), inorganic phosphorus (P), and calcium ion concentrations (Ca++) are expressed in mg. per 100 c.c., age in years, serum protein (Pr) in gm. per 100 c.c., phosphatase (Ph) in King and Armstrong's units, urine pH in units, and basal metabolic rate (BMR) in per cent deviation from normal.

*Abbreviations used for diagnosis:

Atroph., atrophic; Endomet., endometrium; Hyper., hyperplastic; Metrorrh., metrorrhagia; Ov., ovarian; P. I. D., pelvic inflammatory disease; T.B., tuberculous.

TABLE II. RESULTS ON CASES OF PROVED MALIGNANCY

CASE	DIAGNOSIS*	AGE	BLOOD					BLISTER FLUID					URINE pH	BMR
			Ca	P	Pr	pH	Ca ⁺⁺	Ca	P	Pr	pH	Ca ⁺⁺		
1	Met. Ca. of lng. glands	31	11.03	4.22	7.92	5.1	4.6	9.06	3.81	6.12	3.9	4.3	-	-
2	Ca. of urethra	61	10.33	4.09	5.10	3.8	5.4	-	-	-	3.8	-	-	-
3	Ad.-Ca. of ovary	56	9.70	2.00	6.66	8.6	4.5	9.10	1.81	5.64	6.3	4.5	-	-
4	Ca. of cervix	63	9.92	3.10	7.02	5.9	4.4	-	-	-	-	-	-	-
5	Ca. of cervix	62	9.20	2.78	6.69	8.0	4.1	7.83	2.81	5.28	11.7	4.0	-	-
6	Ca. of cervix	55	10.70	3.69	8.40	4.8	4.3	9.22	3.13	6.90	5.3	4.1	-	-
7	Ca. of cervix	69	10.44	4.03	6.57	6.0	4.8	8.65	4.38	4.65	5.4	4.7	-	-
9	Ca. of cervix, metastases	58	9.85	3.44	5.07	9.8	5.2	8.30	3.94	4.20	9.8	4.8	-	- 4.3
11	Ca. of cervix	26	11.00	4.13	7.56	3.9	4.7	-	-	-	3.5	-	-	- 0.4
12	Ca. of cervix	42	10.23	3.41	7.56	7.5	4.3	8.99	3.56	6.27	6.8	4.2	-	- 0.4
13	Ca. of uterus, ascites	65	10.40	3.75	6.12	7.0	5.0	8.80	3.88	4.68	6.8	4.8	-	- 2.8
14	Ca. of cervix, ? met. liver	68	11.10	3.94	6.42	22.9	5.2	9.21	3.78	5.16	17.4	4.8	-	+26.5
16	Ca. of cervix	49	10.45	3.72	6.57	11.3	4.8	8.96	3.77	4.95	9.0	4.8	-	+ 3.3
19	Ca. of cervix and ovary	44	9.00	3.22	4.44	6.5	5.0	7.80	3.25	3.60	7.0	4.8	-	+21.0
20	Ca. of cervix, vagina met.	70	9.61	3.22	5.61	4.0	4.8	7.55	3.30	4.23	3.9	4.3	-	+26.0
25	Malignant lymphoma	18	10.55	3.56	6.96	10.4	4.7	9.50	3.58	6.36	5.8	4.4	-	+ 7.0
26	Ca. of cervix	51	9.85	3.63	6.30	37.8	4.5	8.02	3.81	5.28	27.5	4.2	-	+ 6.0
27	Ad.-Ca. of uterus	63	9.80	2.44	6.48	31.2	4.5	8.73	2.50	5.34	26.1	4.4	-	- 6.1
28	Ca. breast, met. axilla	50	9.82	2.25	7.20	11.1	4.2	8.30	2.46	5.40	7.8	4.2	-	-12.8
29	Ad.-Ca. of ovary	54	10.20	2.68	5.82	12.9	5.0	8.60	2.72	4.62	12.2	4.7	-	+16.0
30	Ca. of cervix	67	8.88	3.22	4.80	4.8	4.7	7.55	3.13	3.63	1.3	4.5	-	+ 8.0
31	Ca. of vagina	49	10.21	2.59	6.57	17.7	4.7	8.65	2.74	5.55	4.1	4.3	-	+ 4.0
33	Ad.-Ca. of omentum	64	9.68	2.61	4.56	27.6	5.3	-	-	-	15.8	-	-	+14.0
36	Ca. of vagina	69	10.08	3.41	6.00	17.1	4.9	8.80	3.56	4.98	12.4	4.7	-	+ 5.5
39	Ca. of cervix, vagina met.	48	9.90	3.81	6.48	8.3	4.5	8.75	3.93	5.58	7.8	4.4	-	- 1.0
41	Ca. of cervix	75	9.92	3.31	6.66	13.5	4.5	8.69	3.41	5.01	10.7	4.5	-	+42.0

TABLE II—CONT'D

42	Ca. of cx., hypertension	83	9.90	3.09	6.60	18.6	4.5	8.33	3.09	5.16	14.4	4.3	6.4	+11.0
43	Ca. of cervix	33	10.00	3.08	7.38	4.9	4.3	8.65	3.69	5.88	4.2	4.1	-	-
45	Ca. of cervix	43	10.30	3.60	7.44	8.3	4.3	8.30	3.94	6.42	5.9	3.8	6.0	+14.5
46	Ca. tube, met. ov. and ut.	57	9.90	4.38	5.22	8.7	5.1	8.12	4.10	4.38	7.5	4.6	5.0	- 1.9
47	Ca. of uterus	53	9.65	3.44	7.02	10.0	4.2	7.93	3.50	6.00	8.4	3.8	4.9	+ 5.0
49	Ca. vulva, met. glands	73	9.92	2.72	6.45	8.7	4.6	8.04	2.97	5.16	8.0	4.2	6.0	+ 1.0
50	Ca. of cervix	37	10.05	3.47	6.72	9.2	4.5	8.74	3.50	6.06	7.7	4.2	5.0	+13.4
51	Ca. of cervix	39	10.17	3.56	6.90	10.4	4.5	8.89	4.10	5.22	8.1	4.6	7.0	+ 4.2
54	Ca. of cervix, metastases	42	10.02	3.88	7.32	10.1	4.3	8.19	3.97	5.94	9.3	4.0	5.4	-13.6
56	Ca. of cervix, met. bladder	34	10.85	3.85	7.98	5.3	4.4	-	-	-	-	-	6.4	+ 8.0
57	Ad. Ca. of ovary, met.	37	10.05	3.31	7.62	3.9	4.2	8.91	3.75	6.24	3.9	4.2	7.6	+ 6.0
58	Ad. Ca. of cervix	36	9.81	3.75	5.28	9.0	5.1	8.57	3.81	4.08	9.3	4.9	5.6	+19.5
59	Ca. of cervix	43	10.40	3.31	6.72	12.6	4.7	8.70	3.34	4.74	11.7	4.7	5.0	+13.0
60	Ca. Cx., Paral. Agitans	58	9.83	3.47	6.66	8.6	4.5	8.42	3.63	5.28	10.5	4.3	6.4	+53.5
63	Ca. Cx., hypertension	57	10.50	3.88	6.69	3.3	4.8	8.73	3.81	5.37	3.2	4.4	6.5	+ 5.5
65	Ca. of cervix	67	10.10	4.28	7.26	8.3	4.4	8.80	4.44	5.94	8.1	4.3	5.3	+21.5
66	Ca. of cervix	37	10.70	3.19	6.60	11.6	4.9	8.83	3.30	5.55	7.2	4.4	4.8	+ 1.2
67	Ca. of cervix, metastases	58	10.85	3.56	7.32	10.7	4.7	9.16	3.47	6.24	11.3	4.3	6.7	+ 3.9
70	Ca. of cervix	50	10.45	3.77	7.05	11.7	4.6	9.04	3.91	6.09	10.5	4.4	4.4	+19.3
71	Ca. of cervix	47	11.35	3.55	7.80	10.2	4.7	9.48	3.55	6.54	9.6	4.3	6.5	- 8.4
72	Ca. of uterus	56	10.68	3.35	7.80	12.6	4.4	8.80	3.42	5.73	12.0	4.3	8.2	- 3.5
73	Ca. of uterus	64	10.95	2.98	7.08	9.9	4.8	9.03	3.58	5.46	9.3	4.6	7.6	+19.8
76	Ca. of cervix	56	9.66	4.31	7.74	8.7	4.0	8.08	4.44	6.18	10.8	3.8	6.4	+ 5.5
77	Ca. of cervix	77	9.50	4.19	6.42	9.9	4.4	7.92	4.69	4.92	10.2	4.2	6.8	- 1.6
Average		52.9	10.15	3.44	6.65	10.6	4.63	8.59	3.54	5.38	9.04	4.38	5.94	+ 8.3

Calcium (Ca), inorganic phosphorus (P), and calcium ion concentrations (Ca⁺⁺) are expressed in mg. per 100 c.c., age in years, serum protein (Pr) in gm. per 100 c.c., phosphatase (Ph) in King and Armstrong's units, urine pH in units and basal metabolic rate (BMR) in per cent deviation from normal.

*Abbreviations used for diagnosis:

Ad.-Ca., adenocarcinoma; Ca., carcinoma; Cx., cervix; Ing., inguinal; Met., metastasis or metastatic; Ov., ovary; Paral., paralysis; Ut., uterus.

be the explanation, as they have not been excluded. However, with this in mind it is of interest to note that in the cancer group there are twelve other cases with definite evidence of metastases, to lymph glands, vagina, and omentum, all of which show normal phosphatase values.

TABLE III. SUMMARY OF RESULTS ON BLOOD AND BLISTER FLUID

	CANCEROUS			NONCANCEROUS		
	MIN.	MAX.	AVE.	MIN.	MAX.	AVE.
<i>Serum</i>						
Ca	8.88	11.35	10.15	9.60	11.03	10.27
P	2.00	4.38	3.44	2.50	4.41	3.40
Pr	4.56	8.40	6.55	4.23	8.10	6.99
Ph	3.3	37.8	10.65	3.9	21.6	7.52
Ca ⁺⁺	4.0	5.4	4.63	4.2	5.2	4.57
<i>Blister Fluid</i>						
Ca	7.55	9.50	8.59	7.90	9.30	8.77
P	1.81	4.69	3.54	2.53	4.41	3.58
Pr	3.60	6.90	5.38	3.54	6.45	5.77
Ph	1.3	27.5	9.04	3.6	20.2	6.94
Ca ⁺⁺	3.8	4.8	4.38	3.6	4.9	4.33
Urine pH	4.4	8.2	5.94	4.6	7.6	5.73
BMR	-13.6	+53.5	+8.3	-12.7	+30.0	+2.5

Calcium (Ca), inorganic phosphorus (P), and calcium ion concentrations (Ca⁺⁺) are expressed in mg. per 100 c.c., serum protein (Pr) in gm. per 100 c.c., phosphatase (Ph) in King and Armstrong's units, urine pH in units and basal metabolic rate (BMR) in per cent deviation from normal.

Values for phosphatase in blister fluid correspond with those for blood but are lower than those for blood in nearly all cases. This indicates that the phosphatase enzyme is diffusible and in the rapid formation of blister fluid by diffusion of intracellular or blood fluids that phosphatase may be found in slightly lower concentrations than those present at the source.

The results of our basal metabolic rate determinations show nothing of interest. While the average figure for the cancer group is higher than the average for the noneancer group this is due to a larger number of high values in the former group. We feel that the number of variables here are too great, as evidenced by the range of -12.7 per cent to +30 per cent in the control group. Certainly no correlation can be established with malignancy per se. The highest value in the cancer group (+53.5 per cent) was obtained on a patient with paralysis agitans and malignancy. We have a few cholesterol determinations on cases of malignancy that confirm previous work¹⁴ and would also indicate that there is no significant change in metabolic rate in cancer.

Similarly the variations of urinary pH in the two groups are so wide that the correspondence of the average figures will give little if any information as to the metabolic processes in either group. We had hoped to find a marked difference in the two groups, if there was a difference in metabolism of a cancerous and noneancerous individual. Our results show that urinary pH may be affected by so many

factors (e.g., dietary, respiratory, temperature, infections, etc.) that the determination is useless as a measure of acid base balance of the body. The one patient with pH 8.2 in Table II had a mild pyelitis.

SUMMARY

This second set of 50 female patients with malignancy and 26 without malignancy shows that no change in calcium or phosphorus metabolism is demonstrable in the blood or blister fluid of persons with cancer. Average protein figures for blood serum are slightly lower in the cancer group, and this will explain why the average calcium figures are slightly lower.

Calcium ion concentrations are normal in malignancy, as we have shown before.

Serum phosphatase is not changed by the malignant conditions here considered. In two patients out of the fifty, we have unexplained high values that may be due to the cancer itself. In another two patients with probable metastases to liver, we have found moderately raised values. In twelve cases of cancer with evident metastases to glands, omentum, or vagina, the serum phosphatase values are normal.

Basal metabolic rate in our cancer cases varies from -13.6 per cent to +53.5 per cent and in our control group from -12.7 per cent to +30 per cent. While average basal metabolism rate is higher for the cancer group, we do not think that this indicates a speeding up of metabolism by cancer.

The pH of a catheterized morning specimen of urine may vary from 4.6 to 7.6 in ward patients without pyelitis and from 4.4 to 8.2 in cancer cases. The difference in the group averages is not significant.

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AN EXPERIMENTAL STUDY OF DISSOLUTION AND ABSORPTION OF RETAINED DEAD FETUSES*

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INTRODUCTION

FETUSES killed experimentally and retained in utero offer an opportunity for study of autolytic processes which occur in an aseptic environment. The rates of these processes in different types of tissue can be compared and the sequence of degenerative changes determined. Such knowledge may have significance in the study of clinical cases in which spontaneous death has occurred. Ballantyne has emphasized that before one can rightly understand the pathology of the dead fetus a clear mental picture must be had of the gross and histologic appearance of the macerative changes. One must construct the common factor of maceration before he can differentiate the special changes due to individual disease in the fetus.

Two major types of material may be utilized in approaching this problem: first, chance specimens from clinical cases and those obtained from various animal dissections; second, material obtained by actual experimentation in which death of the fetus is caused by the investigator under conditions which may be more or less closely controlled. Cases in the first group usually have some pertinent data missing, which increases the difficulty of correct interpretation, a fact generally recognized by those working on such material (see Ballantyne, Greenhill, Meyer, Polak and Beres, Straehnan, Thomsen, and others). Studies on the second kind of material are decidedly few in number in spite of the fact it offers results of a more satisfactory nature (see Fraenkel, Koebner, Kuntz, and Corey).

It is difficult to construct a clear picture of the degenerative changes occurring in a fetus after death, in spite of the many published descriptions dealing with the condition of stillborn young and of dead fetuses retained in utero. Although discrepancies appear in the literature it does not necessarily follow that inaccurate observations were made. It is more probable that insufficient data were on hand. A good deal of the past work was based on specimens found dead in utero. Descriptions of this kind of material have been made for years.

The fault with such material lies in the incompleteness of data which may possibly be related to the dissolution of the fetuses. Such factors as cause of death; whether or not the fetus was normally developed when

*Condensation of the original paper was dictated by lack of space; therefore many of the detailed findings have been omitted.

death occurred; length of retention after death; age of fetus when death occurred; disease and, possibly, the condition of the mother, all may have some effect upon the retrogressive changes. In nearly all the earlier work on fetal dissolution at least one, and generally two or three, of the above factors have been either uncontrolled or not taken into account.

In the present work every attempt has been made to avoid incompleteness or omission of the factors just mentioned. Even with all these precautions considerable unexplainable variation still appeared. However, the data obtained from studying this material are believed to be sufficiently uniform to indicate the general course followed by the retrogressive processes of various fetal structures.

The author is deeply indebted to Dr. Charles R. Stockard and to Dr. Joseph L. Schwind for their interest in and supervision of this work. Acknowledgment is made to the Biology Department of Washington Square College for facilities extended during the early phases of the investigation.

MATERIALS AND METHODS

Young albino rat females were caused to retain one dead fetus. In each case, the fetus was the one nearest the fallopian tube, and it was killed on the fourteenth day after sperm were discovered in the vaginal smear. The operation to kill the fetus consisted in making a medial ventral abdominal incision to expose the uteri. A small incision was made in the uterus just at the periphery of the placenta of the fetus to be killed. A needle with the end bent to form a loop was inserted through this incision and rotated; thus the entire placenta could be freed by this form of curettage. Abortion was prevented by ligating the uterus. Abortion of the litter mates occurred in only two cases and was probably the result of undue mechanical manipulation of the uterus at the time of operation.

In all, 25 fetuses were retained dead in utero for the following periods of time; 12 hours, 1, 2, 3, 4, 8, 9, 11, 14, 15, 17, and 22 days. At the end of the allotted time the portion of uterus containing the dead fetus was removed, sectioned serially, and stained with Ehrlich's hematoxylin and eosin for histologic examination. One fetus of the litter was removed at the time of operation in most cases and fixed as a control.

To determine how soon the type of curettage employed kills the embryo, ten fetuses, from fourteen and fifteen days' gestation to older ones of nearly seventeen days, were treated by this method and taken out of the uterus within 20 to 60 minutes for examination under a dissecting microscope. In no case was the heart beating more than one hour after the operation.

OBSERVATIONS

Variation in degree of development reached by the fetuses was relatively large, although in every instance these fetuses were killed on the fourteenth day of gestation. The stage of development reached was determined primarily by the condition of the lungs, metanephros, and appearance of material around the notochord. The cases were separated into three groups, 12 being within the "mean" degree of development, 5 which might be called "underdeveloped," and 6 which might be classified as "advanced."

The general histologic condition of the entire fetus was determined in each case. Such items as the amount of necrosis, distortion of structures, and organization

of organs were used in making these determinations. As a result of such a study it was readily seen that variation in degree of dissolution occurred for a given length of retention. This agrees with some observations made by Corey.

It also appeared that the "underdeveloped" fetuses were in each case better preserved than those which were further developed yet retained for the same length of time. The fact the fetus is underdeveloped indicates it is progressing slowly, and when this development is stopped experimentally, death may not follow as promptly as in the case of a fast growing fetus. Stockard has shown in somewhat analogous situations that there is less immediate disturbance to the slower developing fetal material. This may explain why in the "underdeveloped" cases there is not as much disintegration in the same length of time.

Two rather distinct types of dissolution were found, which, because of their appearance, were termed "loose" and "condensed." In eight instances the type of dissolution could be definitely termed "loose" and in five other instances "condensed."

The cellular material in the "loose" type appeared loosely held together. There were many small irregular spaces in the fetal tissues; the body cavities were not filled completely by the surrounding material; desquamation of the peripheral tissues generally occurred; this occasionally loosely filled the body cavities. As a result of this type of dissolution the uterine cavity after two weeks of retention contained necrotic debris made up of strips of membranes, small groups of cells and individual cells.

In the "condensed" type of degeneration the organs and structures ran together, filling the body cavities and resulting in a quite solidly packed mass of tissue. Identification of structures was very difficult in this type. After long retention the debris appeared similar to that of the "loose" type. Because of this similarity, separation of the two types was difficult after more than seventeen days' retention.

Determination of the type in progress could not be made until the fetus had been retained at least forty-five hours, nor, due to the slower rate of retrogression, could it be determined in some of the "underdeveloped" cases.

A careful histologic study was made of various fetal structures for each of the retention times previously mentioned. The structures studied were skin, capillaries, endothelium, heart, inner ear, eye, central nervous system, digestive tract, liver, kidneys, gonads, and sclerotome or precartilage. Such a study showed the progressive steps of dissolution resulting from increased length of retention after death and also indicated the respective comparative rates of retrogression existing between these structures.

Desquamation of the epithelium began within twenty-four hours and after seventy-two hours retention was so extensive that it adhered to the fetus only in small areas.

The central nervous system showed some variation in appearance within the same retention times. It may be said, however, that distortion had begun within twelve hours, but it was not until after seventy-two hours that considerable collapse of the system was evident. Although the system was quite disorganized after seventy-two hours the cellular material stained fairly well. This reaction was poor by eleven days' retention. Identification was impossible after fourteen days. The spinal ganglia at first tend to be better preserved than the central nervous system but later, from eight days' retention on, appear similar in condition to the nervous system.

In the case of the eye, the retina appeared to undergo relatively the same processes as the brain and at approximately the same time. The lens underwent dissolution at a slightly more rapid rate than the retina (Fig. 1).

The inner ear underwent disintegration quite rapidly and karyorrhexis appeared to play a prominent rôle. Distortion occurred in cases retained twelve hours, and

by twenty-four hours the cellular organization was poor. This structure was not identified in cases retained longer than fourteen days (Fig. 2).

Distortion or folding of the epithelium of the digestive tract was not common even in cases of prolonged retention and when found occurred in the stomach. In some

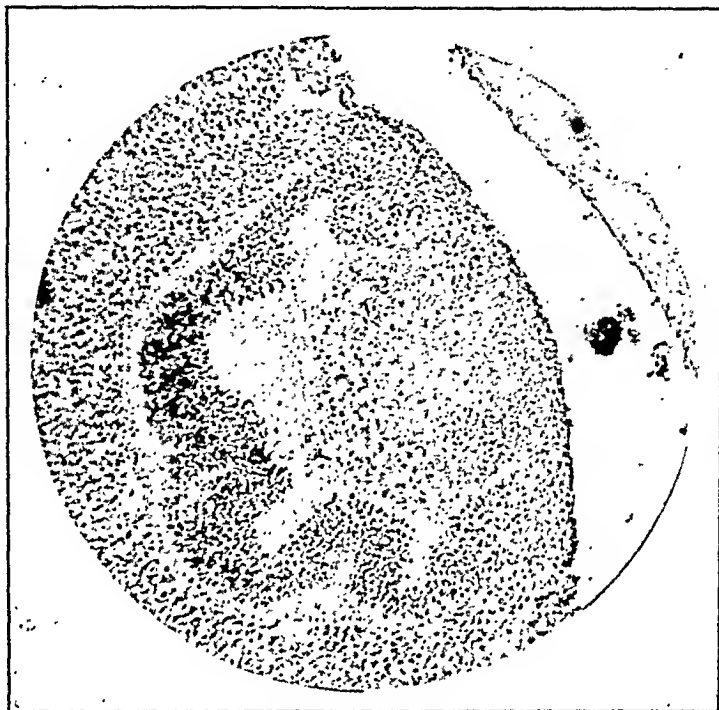


Fig. 1.—Example of the dissolution of lens and retina in cases retained fourteen days.

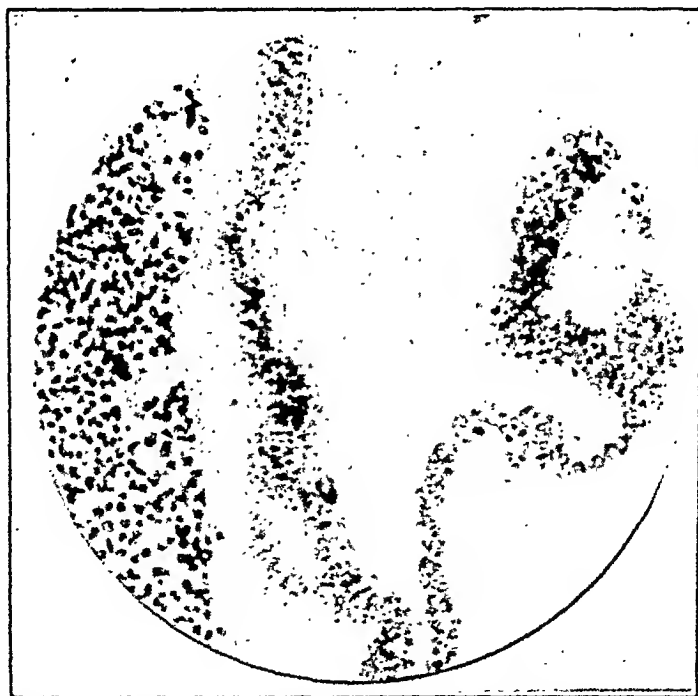


Fig. 2.—The epithelium of the inner ear after eight days' retention.

cases the margin of the epithelium began to be vague and indefinite as early as twelve hours' retention. By forty-eight or seventy-two hours some desquamation had occurred in the esophagus and stomach; however, this was not seen in the intestines.

Indications of karyorrhexis were first noticed in the esophagus after eight days' retention, in the stomach after four days, and in the intestines after three days. This system could not be determined after two weeks' retention except in the "under-developed" cases, and even there it was in a poor state of preservation.

The liver was characterized by a gradual and progressive dissolution in direct ratio to the length of fetal retention. The periphery in most cases, retained forty-eight hours or longer, appeared to have been more greatly affected by the processes of dissolution than the more central areas. This was shown more strikingly, in some cases, in the area lying nearest the placenta. The arrangement of liver cells was somewhat disturbed after twelve hours' retention and after ninety-six hours considerable disorganization had occurred. By fourteen days' retention this organ was quite disorganized and could not be determined after this time except in the "under-developed" cases. The liver had started to spread out and lose its normal shape appearing to have become semifluid in consistency after twenty-four hours' retention. This process was quite advanced after ninety-six hours.

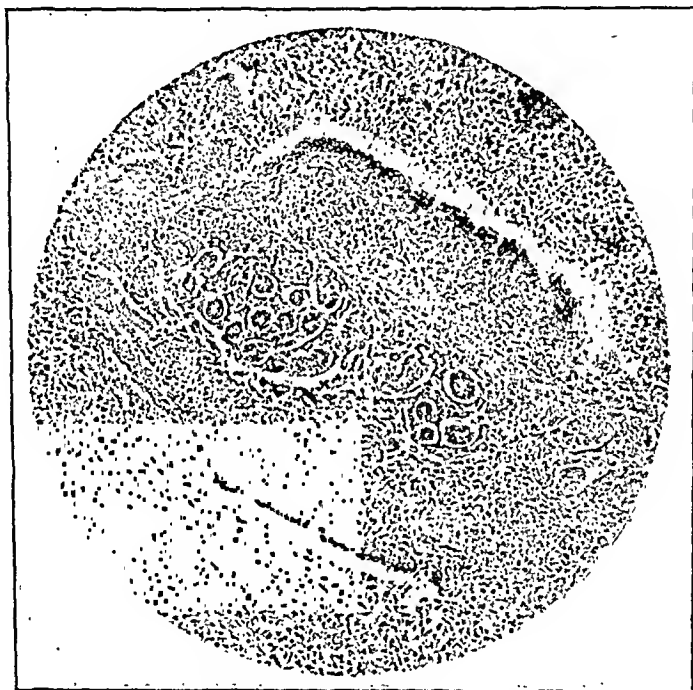


Fig. 3.—Metanephric tubules after being retained twenty-two days.

The general outlines of the kidney tubules persisted remarkably well even after relatively long retention. In the degenerative processes here the cells did not lose distinctiveness abruptly but gradually faded until no longer visible as individual entities. The nuclei began to display some karyorrhexis in the seventy-two- and ninety-six-hour cases. After fourteen days' retention no cell outlines were observable and the nuclei were very lightly stained. In one of the cases retained twenty-two days the kidney could be identified. The material was entirely necrotic but the general tubular arrangement could be seen (Fig. 3).

The endothelium, even after twelve hours' retention, had disappeared from practically all the capillaries, particularly those around the brain and in the dermis. In the larger vessels it had undergone desquamation after forty-eight or seventy-two hours. This was not true of the endocardium.

Very little loss of general organization occurred in the heart at any stage. Even when retained so long in some cases as to lose its affinity for stain the general arrangement, outline, and lumen persisted. After long retention periods the heart

chambers may break apart; yet even when this occurred the general organization of the tissue was relatively well preserved. The endocardium was nearly always present as a continuous lining, although it generally was raised from the underlying muscle. The heart took practically no stain after retention periods longer than fourteen days.

Very little distortion or loss of organization of the cartilage occurred even after long retention, although the nuclei developed irregularities in shape within seventy-two hours. The staining reaction was very poor after nine days' retention.

The relative degree of dissolution and preservation in various fetal structures was determined within the same fetus by histologic examination. Comparisons were made only with other structures of the same fetus. Such comparisons indicate whether or not a structure consistently displayed the same relative degree of dissolution in regard to the rest of the fetus.

The capillaries, epidermis, and inner ear were the most consistent in showing poor preservation. The liver was one of the structures more consistently showing better preservation. While the kidney tubules were quite well preserved in the majority of cases the ratio was not so high as in some of the other organs. They were, however, better preserved than the closely adjacent gonads. The heart, sclerotome, and precartilag were the best preserved of all the structures studied.

Three regions of the central nervous system were compared: brain, anterior cord, and posterior cord. The anterior cord was considered as that portion of the level dorsal to the lungs while the portion at the level of the cloaca was termed as posterior cord.

There were eighteen cases in each of which all three regions could be determined. It was found that the brain was better preserved than the other two regions in 1.85 per cent of the cases. That the anterior cord was better preserved in 7.40 per cent of the cases, while the posterior cord was better preserved than the other two regions in 22.22 per cent of cases. There were, however, 10 instances in which all three regions possessed the same degree of dissolution, or 55.55 per cent of the cases.

Thus, the data indicated that the central nervous system as a whole commonly underwent dissolution at the same rate. However, taking the length of retention into consideration, of the cases in which the degree of dissolution was comparable in the three regions, one-half had been retained for short periods of time. All the cases retained twelve or twenty-four hours, but one, were characterized by an equal degree of dissolution in the three regions.

The cases showing the same degree of dissolution in the three regions were also considered in respect to the general amount of disintegration of the fetus as a whole, and from this view, it appeared that usually these regions were the same in fetuses which were well preserved.

Thus it appeared that all but two of the cases in which the relative degree of dissolution was the same in the three regions of the central nervous system belong to one of the above two categories.

It appears from the foregoing that the three regions tend to be the same in fetuses retained for short periods or in those in which the disintegrative processes are not particularly advanced. This would indicate that the variation which occurred between these regions tends to arise after forty-eight hours' retention and in cases in which such variation occurred the posterior cord was more often the better preserved.

The digestive tract was divided into three regions: esophagus, stomach, and intestines. These were compared with each other in the same fetus in the same manner as was done with the central nervous system. The data thus obtained show the same general tendencies as the central nervous system, although the percentages were slightly different.

There was no actual correlation between the central nervous system and digestive tract in regard to the relative degree of dissolution. For example, cases in which the posterior cord showed little dissolution were not necessarily those in which the intestine was better preserved.

Comparatively, the central nervous system and digestive tract could not be said to belong to either the poorer or better preserved structures.

In the majority of cases the first reaction of the maternal white cells to the presence of dead material in the uterine cavity consisted in migration of polymorphonuclear leucocytes into that region. Later these decreased in number while the lymphocytes increased in number.

Cases in which fetuses were retained from twelve hours to four days showed more polymorphonuclear leucocytes in the uterine wall than cases of longer retention. Variation in numbers present ranged from nearly normal to very abundant, and leucocytes occurred in greatest numbers in cases of three- and four-day retention, particularly in the area of placental attachment. These elements could be traced, moreover, from engorged vessels in the uterine wall to the uterine cavity. Fetuses that had been retained the longest showed practically a normal condition in regard to these cells and gave no evidence of migration such as mentioned above.

Polymorphonuclear leucocytes found in the uterine cavity varied somewhat in number but were usually present in greater amount at about the period of eight or nine days' retention. Their occurrence was most frequent on the periphery of the placenta. Their number decreased in cases retained longer than this and by twenty-two-day retention practically none were present, although the uterine cavity contained considerable necrotic debris.

The lymphocytes began increasing about the time the polymorphonuclear forms had begun to diminish and reached greatest concentration in the uterine wall at eight to eleven days' retention and in the uterine cavity from nine to seventeen days. These elements rarely occurred in cases retained longer than seventeen days.

Numerically the lymphocytes were in no instance equal to the greatest number of polymorphonuclear leucocytes.

DISCUSSION

It must be kept in mind, in any attempt to correlate the present findings with those of previous workers, that earlier studies of this problem were carried out on several different types of animals and that such factors as stage of development of the fetuses, length of retention, and cause of death were not in every case clear. Therefore, great care and some mental reservation must be exercised in making comparisons. The results of the present experiments on fourteen-day rat fetuses, material which heretofore has not been used, are, therefore, not strictly comparable to most results reported in the literature.

There appears to be no questioning the fact that autolysis is the major process concerned with dissolution of dead fetuses. That liquefaction of dead tissue inside the body is actually brought about by intracellular enzymatic digestion was pointed out by Solkowski who named the process "auto-digestion." This process was renamed "autolysis" by Jacoby and established as occurring in retained dead fetuses by Sehlesinger.

Thomsen and Polak and Beres found that in one to ten days the epidermis of stillbirths was raised up in the nature of "blebs" containing serum, and from ten to forty days it was peeling off or absent. A similar condition of "bleb" formation

was seen in the rat, but it occurred within twenty-four hours and at no time was as prominent as described by them. Generally after forty-eight to seventy-two hours desquamation of the epidermis was so great that very little remained on the fetus. In the human being, Strachnan speaks of swelling of the superficial layers of the epithelium, as though these structures were taking up fluid, as one of the first changes in the epidermis. A similar though not so pronounced condition was seen in the rat after twenty-four hours' retention.

With respect to changes in the central nervous system, no histologic description wholly comparable to the one previously given has been found in the literature. Kuntz, in describing a condition in the cat, speaks of the lumen being more or less filled by fragmented cells and tissue débris, but very little was known concerning the history of the fetuses. Somewhat similar conditions were noted in the rat after retention of seventy-two to ninety-six hours.

Polak and Beres mention an altering in shape of the liver through softening during the second stage of from ten to forty days. Thomsen, on the contrary, in speaking of the same stage, claimed that the liver is noticeably soft but retains its shape until removed. In the rat the liver had begun to lose its shape within twenty-four hours, and after forty-eight hours it had begun quite noticeably to spread out to fill the surrounding body cavity.

Greenhill, in describing the liver of a human fetus retained twenty weeks and undergoing mummification, noticed that degeneration was more marked in some areas than in others but did not localize these areas. This point is of some interest as it was found in the rat after forty-eight hours' retention, the periphery of nearly all the livers displayed more advanced dissolution than the medial portions. At present the question as to why there should be regional differences in the amount of degeneration of the same liver cannot be answered. If only a straight autolytic process is involved, the assumption seems warranted that the dissolution should be the same throughout. This condition, however, was not found.

The great variation in the relative amount of dissolution of the liver reported in the literature apparently results, to some extent, from the diverse ages of the specimens studied. Adult livers or those of nearly full-term fetuses undergo rapid maceration while, as shown by the present work, those of fetuses of an earlier stage of gestation do not undergo rapid autolysis. (See Mendel and Leavenworth, Jones and Austrian, Long and Parkes, Vernon, Wells, Thomsen, and Corey).

Thomsen, in describing the kidney, states that from one to ten days the convoluted tubules show marked blurring and the lumen contains detached material; the nuclei are either faintly stained or take no stain at all. From ten to forty days there is widespread karyolysis in the cortex. It must be taken into consideration that he was dealing with stillbirths; the author, on the other hand, was working on rats in which the metanephros was not as well developed. With this qualification in mind it can be said that the present work did not confirm that of Thomsen's. It appears that a considerable difference must occur between the degenerative processes in the kidney of nearly full-term fetuses and in those near the middle of gestation.

The endothelium of the smaller blood vessels disappeared very rapidly and was shortly followed by the disappearance of that of the larger vessels. This is similar to the condition described by Kuntz for the cat. He finds, however, the same condition true for the endothelium of the heart. This finding was not confirmed; on the contrary, the endocardium persisted remarkably well even after long retention.

According to Mall the heart becomes more resistant than the other organs after the fifth week. This is the only reference found dealing with the comparative rate of dissolution in this structure. The present studies confirm his observations, for even when very few other structures can be identified, the heart retains its shape but generally stains lightly.

Various fetal structures were compared with each other in the same fetus in respect to the relative amount of dissolution. The variation between these structures depended upon the rate of the retrogressive changes; especially so since in these cases the processes began at practically the same time in each organ.

The structures studied are listed below in regard to the amount of dissolution, starting with those showing the greatest effects. It must be remembered, however, that this order is not invariably followed and that the list is, therefore, somewhat arbitrary: (1) capillaries, epidermis; (2) ear; (3) lens; (4) retina; (5) brain; (6) esophagus; (7) stomach; (8) gonads, anterior spinal cord, metanephros; (9) posterior spinal cord; (10) intestines, liver; (11) sclerotome, heart; (12) precartilage.

The problem as to what effect the stage of development has upon the dissolution of retained dead fetuses does not appear to be settled at present. Needham states the situation by saying the younger the fetus the more complete the removal and no question arises as to the accuracy of this. In the human being, both Pigeaud and Thomsen point out that in the first stages of development or in premature fetuses maceration is more rapid than in cases of full term. It is difficult to see how this is brought about in view of the work of Vernon, Jones and Austrian, and Mendel and Leavenworth. They agree that as fetal life progresses enzyme activity becomes increasingly effective. If this factor is taken into consideration, autolysis should proceed more slowly in fetuses which have had a retarded development. This is in accordance with the data on hand.

There appears at present no correlation between the "loose" and "condensed" types of dissolution and the rate of disintegration, since the latter is approximately the same in both cases.

The "condensed" type appears to have had its fluids extracted, resulting in the cells of the entire fetus lying compactly together with practically no intercellular spaces or body cavities. This process is not similar to mummification and the only report seen which describes something resembling it is that of Koebner, who speaks of a "dry retrogression" in which the fetal tissues run together and identification of structures is very uncertain.

The "loose" type is the more common and conforms to the general descriptions of macerating fetuses.

The definite causes underlying these two types of dissolution are as yet undetermined. As far as is known the experimental procedure was the same throughout.

In the present work, nuclei could be seen in cases of over two weeks' retention. This does not support Well's statement that fetuses which have undergone aseptic autolysis in the uterus show a complete loss of nuclei in five or six days.

There appears to be some contradictory evidence as to the chemotactic influence exerted on leucocytes by dead material. Bradley, in discussing dead tissue in the body, states that phagocytosis is secondary to autolysis, occurring after the tissue is broken down and some substance formed which sets up a chemotactic attraction. Amino acids are a part of the end products of autolysis, and Wolf found that such acids are positively chemotactic to a certain extent. However, Wells states that chemotactic substances do not seem to be formed in aseptic dead tissues and that the absence of leucocytic infiltration is so marked that it seems possible that substances with negative chemotactic effect are present.

In the present work, leucocytic migration to the uterine cavity did occur to some extent in cases of shorter retention but was negligible in fetuses retained for longer periods of time. In event of migration, concentration of leucocytes was greatest on the periphery of the placenta and consisted mainly of polymorphonuclear cells. It would thus seem that these appeared in response to either the mechanical injury to the uterine wall and placenta or to some influence exerted by the dead placenta. However, their presence was of short duration, for after eight or nine days very few were found although the placenta was still present.

In cases of longer retention the uterus contained a good deal of necrotic and presumably autolyzing material. There were no polymorphonuclear leucocytes, yet this material was not enclosed by intact membranes and was therefore free to exert a chemotactic attraction for polymorphonuclear leucocytes, which is in agreement with Well's above observation. It appeared, moreover, that only a slight attraction for lymphocytes developed.

Few investigators working on dead fetuses have paid attention to the time at which autolytic processes are initiated. Kuntz and Corey, in studying fetuses retained dead in the uterus, concluded that considerable time must elapse before the processes became apparent. Long and Parkes, however, found that changes could be seen after incubating rat, mouse, and pig fetuses in Ringer's and under toluene for thirty-four hours. Nicholas, on the other hand, placing eight- to nine-day rat fetuses with undisturbed embryonic membranes in Ringer's and Locke's physiologic saline at body temperature for at least six hours, found no changes occurred, but after twelve hours considerable disintegration was in evidence.

Disintegrative changes had begun in the fetuses studied in the present work after twelve hours' retention in utero. Such changes, although not considerable, were, nevertheless, quite definite. It thus appears that the data on initiation of autolytic processes appearing in this report agree fairly closely with those of Nicholas on ineubated fetuses.

According to Long and Parkes and Corey the liver and gastrointestinal tract are the first to show the effects of macerative or disintegrative processes, and Corey further states that the changes spread from these structures to the other organs. This is not confirmed by the present work. All the fetal structures of cases retained twelve hours appeared to be practically the same in respect to retrogressive changes, with the possible exception of the dermis, ear, and capillaries. Thus, it would seem that the autolytic processes had begun in the various structures of these fetuses at practically the same time and did not spread from some more or less localized point as indicated by Corey. It should be kept in mind, however, that the present work was done on fourteen-day fetuses whereas Corey worked on those near full term, and hence the two lots of material are not strictly comparable.

Although there is contradictory evidence as to the time and place autolysis is initiated, there appears to be a uniformity of opinion that it proceeds at different rates in different structures. While it is generally accepted that the rates vary, not all workers agree as to the amount of variation nor as to the structures showing it. It should be pointed out that in the present work the retrogressive changes at first appeared to be synchronous in the fetal structures and that differences in amount of dissolution occur secondarily.

It is interesting to note the excellent condition of the females carrying a dead fetus. They not only nursed litters in a perfectly normal manner but would come into estrus, characteristic of the unoperated female after removal of her litter. This behavior was typical even though a dead fetus was being carried in one horn of the uterus.

Appearance of estrous changes in the vaginal smears suggested the possibility that these females could become pregnant while still absorbing a dead fetus in one uterine horn. This was confirmed in the one case tested, pregnancy resulting in a litter of two. Of interest in this connection is a case reported by Løvset and one by Thoms, in the human being, in which a female became pregnant while the uterus contained a dead fetus.

SUMMARY

1. An experimental method is described for the study of retrogressive changes in retained dead fetuses in the rat.
2. The initiation of retrogressive changes in the dead fetus occurs early, within twelve hours.

3. The respective rates of dissolution of most of the formed elements of the fetus are uniform up to twenty-four hours' retention, after which time variation becomes apparent.

4. Aside from described exceptions, the fetal structures in fourteen-day rat embryos can be enumerated as follows, starting with those showing the greatest amount of dissolution: (a) capillaries, epidermis; (b) ear; (c) lens; (d) retina; (e) brain; (f) esophagus; (g) stomach; (h) gonads, anterior spinal cord, metanephros; (i) posterior spinal cord; (j) intestines, liver; (k) sclerotome, heart; (l) precartilag.

5. Two types of dissolution are described as quite apparent in the early stages of retention; "loose" and "condensed." In later stages the distinctive characteristics of these two types become gradually obscured.

6. Evidence is offered of a chemotactic influence of the retained material toward leucocytes of maternal origin during the early stages of retention. This chemotaxis is not apparent in later stages.

7. It is possible for a female to become pregnant and to produce normal young while retaining a dead fetus.

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The author ligated the uterine tubes of rabbits with silk and with fresh aponeurotic sutures. He killed the animals at periods varying from one to seven months and found that within the first thirty days the lumen of the tubes was found completely obliterated at the site of ligation. However, in those sacrificed after thirty days, canalization of the tubes had been reestablished.

AUGUST F. DARO.

A BIOLOGIC TEST FOR THE DIAGNOSIS OF INTRAUTERINE FETAL DEATH*

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THE diagnosis of intrauterine fetal death is difficult, especially before the fifth month of gestation. Horner¹ has shown the x-ray is of no value before the fifth month because osseous development is slight. After osseous development is demonstrable by the x-ray, according to the work of Matthews,² and Stein and Arens,³ the fetus usually must be dead from four to five days before enough degeneration of the brain tissue takes place to cause overlapping of the skull bones or asymmetry of the head, and ten to fourteen days are usually required for collapse of the thoracic cavity and horseshoe curvature of the spine. They have also shown that decalcification of the bones is not a reliable sign of fetal death, as errors in technic may give similar light areas. Since overlapping of the skull bones may occur during labor or with engagement of the head, it is not a very reliable sign. Falls⁴ has shown that fetal heart tones may be heard with the vaginal stethoscope as early as the fourth month, and if after this stage of gestation heart tones or fetal movements cannot be heard, he considers this strong presumptive evidence of fetal death.

The object of this paper is to set forth our experience in the diagnosis of intrauterine fetal death, using the Schneider⁵ modification of the Aschheim-Zondek reaction. The value of a test of this type is especially great in the early months of gestation, and in the later months of gestation, the reaction can be obtained twenty-four to forty-eight hours after the death of the fetus.

TECHNIC

Ten cubic centimeters of a fresh voided morning specimen of urine are filtered and injected into the marginal vein of the ear of a thirteen- to fifteen-week-old-virgin female rabbit, weighing between 4 and 5 pounds. From forty to forty-eight hours after injection of the urine, the rabbit is sacrificed and autopsied. Upon gross inspection of the rabbit ovaries, various reactions may be seen. It is advisable to examine the ovaries immediately after killing the rabbit before postmortem changes have set in. If the ovaries are opaque, cylindrical, and flat with no mature follicles, they are too immature to respond to the hormonal stimulus of the urine, and the test

*Presented at a meeting of the Chicago Gynecological Society, March 20, 1936.

should be repeated. If the ovaries are rounded and contain one or more mature follicles that contain no hemorrhage, the test is negative. Should the follicles contain peripheral hemorrhage as shown in Figs. 1 and 2, the diagnosis of intrauterine fetal death may be made. One cannot differentiate by this method between retained placental tissue with the fetus expelled and the dead fetus still in utero. The same reaction is found whether a dead fetus or chorionic villi are in the tube, abdomen, or uterus. This reaction we have termed the dead fetus reaction. If the follicles are hemorrhagic throughout, the test is positive (Fig. 3).

In order to facilitate description of the cases in which the dead fetus reaction was obtained by using the above-mentioned method, the cases have been divided into seven groups. All the patients in each group have similar histories and physical findings.

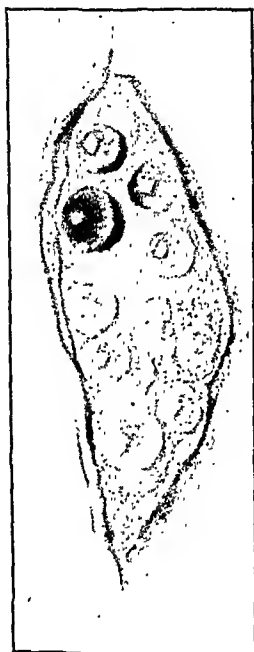


Fig. 1.

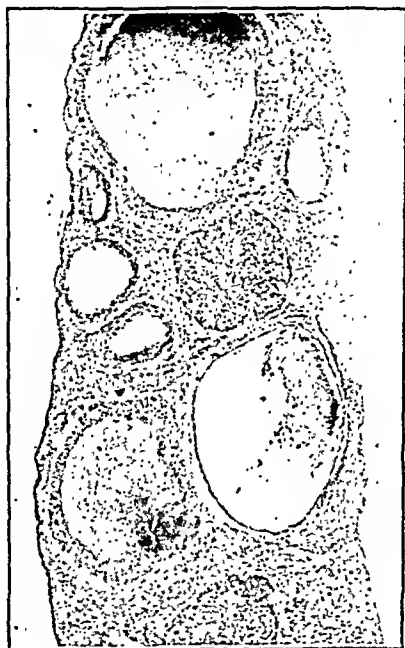


Fig. 2.

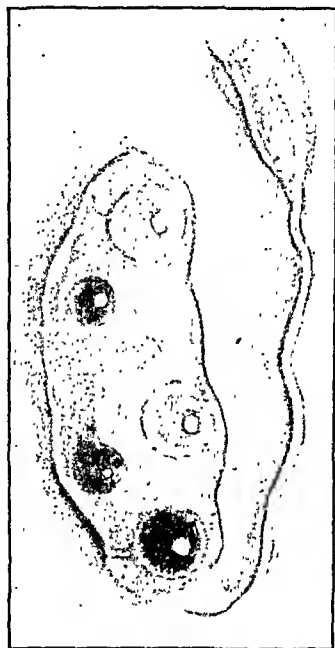


Fig. 3.

Fig. 1.—Drawing of an ovary from a dead fetus reaction, showing peripheral hemorrhage in the follicle.

Fig. 2.—Microphotograph showing peripheral hemorrhage in the follicle.

Fig. 3.—Drawing of positive reaction showing hemorrhage throughout the follicle.

1. In Group 1 the following case history is characteristic of the group:

CASE 1.—H. N., white, female, thirty-two years of age, grav. i, para 0, who had menstruated regularly until July 24, 1933, when she missed her period. She took large doses of castor oil and quinine early in August and three weeks later began to bleed vaginally. A rabbit was injected in the usual manner and a dead fetus reaction obtained. A diagnosis of incomplete abortion was made and the patient was curetted. Curettage revealed some degenerated placental tissue.

We had 18 similar cases in which, in an effort to produce an abortion, the patient took castor oil and quinine or some ergot derivative and succeeded in producing an incomplete abortion. The pregnancy

was proved by findings on curetting the uterus. In each case the dead fetus reaction was obtained before completion of the abortion, and in all cases we were able to find placental tissue in the clots passed on after curettage.

2. Group 2 is best described by the following case:

CASE 2.—Ko., aged twenty-four years, para i, grav. ii, was observed seventy-two days after the first day of her last menstrual period. The uterus had not increased in size after eight weeks of gestation. No bleeding or signs of fetal death were present. A rabbit was injected in the usual manner, and a dead fetus reaction was obtained. A dilatation and curettage were done, and degenerated placental tissue was found.

We have had 8 similar cases all giving the same results, 2 occurring in the first trimester of pregnancy and 6 occurring in the second trimester.

3. In the third group there are 15 cases in which urine was taken from the bladder by catheter on the delivery table after the patient had delivered a macerated stillborn child, and 10 c.c. was injected into a rabbit. In all these cases patients entered the hospital in labor and gestation varied from the fifth month to term. In all cases a dead fetus reaction was obtained. This was done in order to determine the reliability of the reaction in cases with a known dead fetus.

4. In Group 4 we have all patients who entered the Research and Educational Hospital with a diagnosis of threatened abortion.

It is a routine procedure at the Research and Educational Hospital to run a Schneider modification of the Aschheim-Zondek tests on all patients entering the hospital with the diagnosis of threatened abortion to determine whether or not there is a live fetus in utero. Efforts are made to retain the fetus in utero until a reading of the rabbit ovaries can be made. If the test shows the dead fetus reaction, sedative therapy is stopped, and the patient is allowed to abort. We have had 23 dead fetus reactions in these tests and each expelled macerated fetus or placental remnants twenty-four to seventy-two hours after therapy was stopped, 15 occurring in the first trimester of pregnancy and 8 in the second trimester.

5. Group 5 is the ectopic gestation group, and the following case history is characteristic:

CASE 3.—Br., twenty-five years of age, para ii, grav. iii, entered the hospital complaining of pains in the right lower quadrant of five days' duration. Slight enlargement of the right tube was found upon bimanual examination. Forty-two days had lapsed since the first day of the last menstrual period. An injected rabbit revealed a dead fetus reaction. A laparotomy was done and decidual tissue, but no fetus, was found in the right tube. There have been ten other cases with similar histories, similar findings on bimanual examination and all gave the dead fetus reaction. At operation all had placental tissue in one of the tubes.

6. In Group 6 we have patients who entered the hospital for treatment of eclamptogenic toxemia. At the time of their admittance the fetal heart tones were audible but disappeared later. The following case best illustrates this group:

CASE 4.—M. H., aged twenty-nine years, grav. v, para iii, seven months' gestation, entered the hospital with preeclamptic toxemia. The blood pressure was 200/130, 4-plus albumin, and many casts and red cells were found in the urine, and the phenolsulphonephthalein test showed 0 per cent at the end of two hours. The fetal heart tones were heard upon entrance to the hospital, but two days later disappeared. A rabbit was injected with the patient's urine in the manner described and autopsied forty-eight hours later. A dead fetus reaction was obtained. The patient went into labor four days later and delivered a somewhat macerated fetus. There were 4 patients in the group and all in the last trimester of pregnancy.

7. In Group 7 there are included the patients who had several tests run at intervals varying from two to seven days. In each case the fetus was retained in utero for longer than a week and all occurred in the last trimester. The following history is quite typical of the group:

CASE 5.—V. B., para i, grav. ii, entered the hospital on Oct. 10, 1934, with a diagnosis of preeclamptic toxemia. Examination revealed a colored female in the ninth lunar month of gestation, with a blood pressure of 200/110, a phenolsulphonephthalein of 50 per cent at the end of two hours, fetal heart tones 132, and a 3-plus Kahn test. The fetal heart tones were heard daily until November 10, when they were not heard. A rabbit was injected on November 11, 13, 15, 18, 20, and 23. The test at each time showed a dead fetus reaction except on the eighteenth when it showed a distinct positive. Here we had a false positive.

In all cases the pregnancy was terminated by the expulsion of a badly macerated fetus. In this group there were 4 cases. One had 3 tests over a period of ten days, another 3 over twelve days, another 4 over a period of fifteen days. The fourth case has been described. There was only one false reaction in this group.

The next 3 cases do not fall into any of the 7 groups but each has a special point of interest.

CASE 6.—E. MeB. delivered a normal child but failed to expel the placenta. Manual removal was thought inadvisable, and the patient was put to bed with the placenta in utero. Rabbits were injected with 10 c.c. of urine on the seventh, eleventh, eighteenth, twenty-sixth, and thirty-second postpartum days. The test on the seventh, eleventh, eighteenth, and twenty-sixth days showed a dead fetus reaction. The test done on the thirty-second day showed a negative reaction. On the twenty-fifth day a small piece of grayish tissue was expelled and was found to be degenerating placental tissue. On the thirty-second postpartum day a sterile vaginal examination was done and no evidence of placental tissue was found. From the seventh to the thirty-fifth postpartum day, the patient had temperature varying between 100° to 106.4°. It was assumed that all the placental tissue was either absorbed or expelled between the test taken on the twenty-sixth and the third-second postpartum days.

CASE 7.—Ko., para i, grav. ii, aged twenty-six years, forty-one days after the first day of her last menstrual period, began to bleed vaginally and this bleeding

continued for two days. A rabbit was injected to determine whether or not the fetus was alive. A dead fetus reaction was obtained, but because the clinical history was more in keeping with a live pregnancy, a conservative attitude was taken. Two weeks after the first test a second was done and this time it was positive. The patient went to term and delivered. In this case we have a false dead fetus reaction where the fetus was alive.

CASE 8.—Hi., aged thirty-two years, para i, grav. iii, was observed in the thirty-second week of her gestation. Fetal heart tones were not heard after this time. X-ray picture of the fetus in utero did not show characteristic overlapping of the skull bones or any evidence upon which one could diagnose a dead fetus. A rabbit was injected in the usual manner and a dead fetus reaction was obtained. The patient failed to go into labor following two attempts at induction with the Watson technique. A Voorhees' bag was inserted into the cervix; the patient went into labor and delivered a macerated fetus four days after the dead fetus reaction.

Jeffcoat⁶ of England reported a series of 9 cases similar to this series, using mice instead of rabbits. In his series he was able to predict termination of the pregnancy by the expulsion of a dead fetus 7 times. He, however, believed the reaction observed was due to an upset in the hormonal balance, there being a relative excess of estrin over prolan A and prolan B. He also thought the reaction was not indicative of fetal death but of an impending abortion due to the hormone imbalance.

Tate⁷ using rats confirmed Jeffcoat's observations with a series of 7 cases with 6 accurate results. Jeffcoat's belief that the reaction was due to impending abortion rather than fetal death is not substantiated by this work. All his cases occurred early in pregnancy when a diagnosis of fetal death is difficult.

In our work in cases of premature labor, where the pregnancy was far enough along to hear fetal heart tones, we were unable to obtain a dead fetus reaction as long as fetal heart tones were audible, but twenty-four to forty-eight hours after the fetal heart tones disappeared the dead fetus reaction was obtained. This, plus the macerated condition of the fetuses upon expulsion and the fact the retained placental alone can give the reaction, has led us to believe that this is the result of fetal death rather than of impending abortion. From our work we are unable to state the causative factors for this reaction.

Bishop⁸ has come to the conclusion that pregnancy tests depend on the presence or absence of functional chorionic tissue and not upon the life or death of the ovum. In our work we have occasionally observed positive Aschheim-Zondek reactions where there were no functioning chorionic villi. They have been observed in teratomas of the ovary and testes, dermoid cysts of the ovary, and serous cysts of the ovary.

To rule out the possibility of a fading reaction, the urine of 5 women postpartum was injected into rabbits, and all the reactions observed were either negative or positive and none yielded the dead fetus reaction. The reaction became negative twenty-four to seventy-two hours after the birth of the fetus. Dilution of the urine of 5 pregnant women was also tried, but here again the results were negative or positive. A positive reaction was observed with as little as 1 c.c. of urine and negatives with as much as 5 c.c. of urine, using the same technique.

CONCLUSIONS

1. Using the Schneider modification of the Aschheim-Zondek test, we have been able to obtain the dead fetus reaction with an accuracy of 95.3 per cent in a series of 86 cases.

2. The test is positive for dead fetus reaction as long as living chorionic tissue is in contact with the maternal blood.

3. Its value in ectopic pregnancy lies in establishing the fact of fetal death and, inasmuch as further growth is then arrested, affording information that the danger of rupture or abortion is decreased.

4. The reaction is not positive when postpartum or diluted antepartum urine is used for the test.

5. While not infallible, it is extremely valuable and should be used in conjunction with the clinical reactions in determining treatment in a given case.

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1817 W. POLK STREET

DISCUSSION

DR. A. E. KANTER.—This study is of interest, particularly in its reference to the work I have been trying to do on fish. We believe that the reaction in the fish test is the effect of the estrogenic agent, which does not decrease in the urine as quickly as does the prolan. We have had seven negative Friedman tests and seven positives in fish in cases proved at operation to be ectopic pregnancy.

If the test follows the same rule as it does in the fish, I am quite sure we are safe in saying that it is the estrogenic content which brings down the ovipositor and gives the findings Rezek described.

DR. REZEK (closing).—The test I have described will be valuable, particularly in cases of ectopic pregnancy to indicate which should be operated upon immediately and which could be treated conservatively. So far one patient has been treated conservatively. From a bimanual examination and history of this dispensary patient, a diagnosis of ectopic pregnancy was made and surgery was suggested, but the patient refused. We obtained a urine specimen and a dead fetus reaction was noted. Five tests in all were run, the last being negative. We have no proof that this patient had an ectopic pregnancy, because she was not operated upon, but there was good clinical evidence on which to base a diagnosis of ectopic pregnancy.

CARCINOMA OF THE BODY OF THE UTERUS*

A REVIEW OF 279 CASES WITH FIVE-YEAR END-RESULTS IN 211 CASES

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CARCINOMA of the fundus of the uterus is a frequent and highly malignant neoplasm. Within the last few years many statistical studies based on the value of different methods of treatment and of diagnosis have appeared. The following study was undertaken in an endeavor to check the results in our own series of cases.

MATERIAL

From Jan. 1, 1900, to Jan. 1, 1935, 279 patients suffering from carcinoma of the body of the uterus were admitted to the Hospital of the University of Pennsylvania. In this entire group the diagnosis was verified by histologic examination. Of the 279 patients, 211 were admitted five or more years before 1935, and these form the basis for the five-year, end-result investigations. In this group of 211 patients 5 are included in whom it was impossible to determine whether the carcinoma had its origin in the uterus or in the ovary. In view of the fact that a number of the old case histories were incomplete, some discrepancy in the number of cases will be noted in the various groups. Of the 211 patients admitted five or more years ago, 171 (81.0 per cent) have been followed and the results noted. All untraced patients are regarded as having died of carcinoma.

Age on Admission.—Table I shows the age on admission in 268 cases. Although carcinoma of the fundus may occur at any age, in our series the greatest number of

TABLE I. AGE ON ADMISSION FOR TREATMENT

AGE IN YEARS	PATIENTS	
	NUMBER	PER CENT
20-29	4	1.5
30-39	18	6.7
40-49	49	18.3
50-59	124	46.3
60-69	57	21.3
70-79	16	5.9
Total	268	100.0

patients, 124 (46.3 per cent), were between the age of fifty and fifty-nine. The youngest patient was twenty and the oldest seventy-six. Twenty-two patients (8.2 per cent) were under forty years of age.

*Read at a meeting of the Brooklyn Gynecological Society, March 6, 1936.

Menopausal Status.—Carcinoma of the fundus is often considered a postmenopausal disease, but of our cases, 80 patients (30.5 per cent) were in the premenopausal age as compared to 182 (69.5 per cent) in the postmenopausal age.

The Relation of Frequency of Childbearing to the Development of Fundal Carcinoma.—An analysis of the marital status showed that 223 patients were married and 55 were unmarried. In one, the status was not mentioned in the history. Of the 223 married patients, 150 (67.3 per cent) had undergone one or more full-term deliveries, whereas 48 (21.5 per cent) were nulliparous, and in 25 (11.2 per cent), parity was not known.

TABLE II. FREQUENCY OF CHILDBEARING IN RELATION TO DEVELOPMENT OF FUNDAL CARCINOMA

PREGNANCIES	PATIENTS	
	NUMBER	PER CENT
0	48	24.2
1	32	16.2
2	32	16.2
3	34	17.1
4	19	9.6
5	33	16.7
Total	198	100.0

Table II exhibits the number of full-term pregnancies in the 198 cases. In this series of cases parity played but a small part as a predisposing factor in the development of the carcinoma. The condition was relatively about as prevalent in those who had borne children as in those who had not. Nor was the number of children borne to each patient significant.

Chief Symptoms.—Metrorrhagia is undoubtedly the most important symptom of carcinoma of the uterine fundus. Although this type of bleeding may be the result of a benign condition, its presence demands immediate investigation in all cases. Hemorrhage was the first symptom observed in 80.5 per cent of the patients, and leucorrhea was noted in 10.3 per cent. The onset of bleeding and leucorrhea occurred simultaneously in 8 per cent of the patients. In 72.9 per cent of the patients the bleeding was predominantly of the intermenstrual type and was the most prominent symptom. In only 17.9 per cent was the metrorrhagia associated with menorrhagia, whereas menorrhagia alone was present in 6.8 per cent.

In the metrorrhagia the flow was usually scanty at the onset, but in a majority of patients it soon became moderate or profuse. In 30.9 per cent of the patients the bleeding was associated with a leucorrheal discharge. This was slight at the onset, but later became more profuse, foul, and in many of the cases irritating.

Although many of the patients comprising this series were in the advanced stage of the disease, only 58 (22.1 per cent) complained of pain.

Duration of Symptoms.—The average duration of symptoms prior to the onset of treatment was 17.9 months. In those patients who were still menstruating, the average duration of symptoms was 22.2 months as compared with sixteen months in the postmenopausal cases. Table III gives the duration of symptoms.

TABLE III. DURATION OF SYMPTOMS BEFORE BEGINNING OF TREATMENT

DURATION OF SYMPTOMS IN MONTHS	PATIENTS	
	NUMBER	PER CENT
Less than 12	113	43.8
12-23	75	29.1
24-35	13	5.0
Over 35	57	22.1
Total	258	100.0

Only 113 (43.8 per cent) of the patients sought treatment prior to one year after the onset of symptoms. In 96 cases the carcinomas were associated with myomas, and in this group the average duration of symptoms was 21.8 months, or 3.9 months longer than the duration of symptoms for the whole series. It was also observed that in those patients with myomas who had passed the menopause the duration of symptoms was nineteen months, as compared to sixteen months for the postmenopausal group in the whole series. Furthermore, the patients in the active child-bearing period who had associated myomas, the average duration of symptoms was 28.1 months as compared to 22.2 months for the patients in the entire series.

The association of myomas increases the difficulty of determining the presence of fundal carcinoma, and in our series it seemed to result in delay in seeking medical advice.

TABLE IV. ACCURACY OF PREOPERATIVE DIAGNOSIS

DIAGNOSIS	PATIENTS	
	NUMBER	PER CENT
Positive	184	67.9
Suspected	45	16.6
Unsuspected	42	15.5
Total	271	100.0

Preoperative Diagnosis.—Thus in 87 cases the diagnosis was actually dependent upon histologic examination, and in 42 of these the presence of a malignant neoplasm was unsuspected.

It is worthy of note that in the unsuspected group, 16 of the 42 cases of carcinoma developed in myomatous uteri, thus emphasizing the frequent association of these two neoplasms and also the increased difficulty of arriving at an accurate diagnosis in this type of case. The fact that nearly one-third of the cases in this entire group were not recognized prior to operation, and that 15 per cent of them were totally unsuspected until a microscopic examination had been made, shows the necessity for making routine histologic studies of all specimens of endometrium removed by curettage. It must be stated here that carcinoma of the fundus can never be recognized with certainty until the uterus is available for macroscopic inspection or until histologic examination of curettings can be performed. Cases that occur before or during the menopause or that are associated with uterine myomas are especially likely to give rise to confusion. Furthermore, the earlier the stage of advancement, the less positive is the preoperative diagnosis, and the greater is the likelihood of securing a permanent cure, provided the correct diagnosis is arrived at and treatment instituted.

Our studies also demonstrate the importance, in all cases of supravaginal hysterectomy, for supposed benign conditions of making an inspection of the endometrial cavity before closing the abdomen.

In cases in which the macroscopic diagnosis is in doubt, a frozen section should be examined before the abdomen is closed, so that the surgeon may perform a complete operation if carcinoma is found to be present.

The Reliability of Histologic Diagnosis.—If a sufficient amount of material is available for study, the histologic diagnosis should be correct in almost 100 per cent of the cases.

Paraffin sections of curettings may be prepared and made ready for histologic examination in twelve hours; these form the most satisfactory method of histologic examination for routine employment. When the curettings are abundant and an immediate hysterectomy is contemplated, one or more large pieces of tissue may be cut by frozen section. If the examination of the frozen section is positive for carcinoma, the diagnosis of malignancy may be accepted; if, however, the result

is negative, all the remaining tissue, including the remains of the frozen section block, should be cut by the paraffin method before carcinoma is excluded. When only a small amount of tissue is available, or when the tissue is secured in small particles, frozen sections are not satisfactory. When cutting paraffin blocks, it is important to cut at different levels in order that a particle of each piece of tissue may be available for histologic examination.

In the Laboratory of Obstetric and Gynecologic Pathology at the Hospital of the University of Pennsylvania no case during the last thirty-six years was diagnosed as carcinoma as the result of examination of the curettings that did not, when the uterus was subsequently removed, confirm the original diagnosis. Likewise, so far as we know, no case that was originally diagnosed as benign was later shown to be malignant. These statements are made in order to show that the histologic diagnosis of carcinoma of the fundus based on the examination of curettings is, when made under good conditions, reliable. It is needless to emphasize the hazards that may result from inexperience on the part of the pathologist, and it should be stressed that a histologic diagnosis based on the examination of curettings requires special knowledge and training.

Associated Pathology and Metastases.—Perhaps the outstanding feature in this series of carcinomas was the high proportion of cases found to be associated with uterine myomas, 34.9 per cent (96 cases). Other things being equal, it may be assumed that in those cases associated with myomas the prognosis would be better because of the increased thickness of the uterine wall, as the integrity of the myometrium is generally regarded as the chief feature on which to base the prognosis. However, probably the greater difficulty of diagnosis and the increased hazards of operation counterbalance this theoretic advantage.

Metastasis, or transtubal involvement of one or both ovaries, was present in 19 cases: the right ovary was involved in 3, the left in 6, and both ovaries were affected in 10 specimens.

The tubes were the seat of metastases or extension in 5 patients. In 8 instances, the omentum, intestines, epiploic appendages, mesosalpinx, or pelvic lymph glands were known to have been invaded.

In 15 patients extension to the parametrium was present on admission.

Sampson believes that transtubal implants occur, and as an initial step in all hysterectomies which are to be performed for known or suspected cases of fundal carcinoma, he has recommended the ligation of the tubes in the region of the ampulla in order to prevent any invasion of the abdominal cavity.

TREATMENT

It will be realized that in attempting to analyze the end-results secured in a group of cases that extend back over a period of thirty-five years many difficulties will be encountered, not the least of which are the various methods and modifications of treatment that may have been utilized. During the period covered by this analysis neither preliminary irradiation nor postoperative roentgen ray therapy was used routinely in the treatment of these cases. For comparison the cases may be divided into two main groups, namely: (1) Those treated by hysterectomy and (2) those treated by radium.

Of the 211 patients, all but 7 received treatment; four of the latter were believed too far advanced and three refused treatment. All the patients that were considered too advanced for treatment were seen prior to 1910 with exception of one patient. Today these would probably be given the advantages of irradiation either by

means of radium or roentgen ray or both. Previous to 1930 our radium dosage was not standardized, and often did not average over 2,400 or at most 3,000 mg. hours with a screening of either 2 mm. of aluminum, or brass or 0.5 mm. of platinum. Today as a minimum we use 4,800 mg. hours of radium with a screening of 1 mm. of platinum and 2 mm. of rubber, followed by deep roentgen ray therapy.

OPERATIVE MORTALITY

Under this heading are included all deaths that occurred in the hospital following treatment. Table V shows the mortality.

TABLE V. OPERATIVE MORTALITY

METHOD OF TREATMENT	PATIENTS		
	NUMBER	OPERATIVE DEATHS	
		NUMBER	PER CENT
Hysterectomy	115	5	4.3
Radium	89	2	2.2

Operative mortality for combined series, 3.4 per cent.

The five deaths that followed hysterectomy were all due to peritonitis. One of the deaths in the radium series was due to cardiac failure and occurred within a few hours after treatment; the other death was due to peritonitis. It is questionable whether either of these deaths should be attributed to the irradiation. Furthermore, in considering the mortality it should be remembered that the routine treatment consisted of hysterectomy, and that radium irradiation was generally employed only when some contraindication to the performance of hysterectomy was present, so that the group treated by radium irradiation practically consisted of all the bad risks in the entire series.

FIVE-YEAR SALVAGE

For purposes of comparison of the methods of treatment, a five-year survival period has been selected. Included in this are certain patients who are known to have been suffering from recurrences or that developed these at a later date.

Table VI shows the total five-year salvage and is based on the number of patients seen.

TABLE VI. FIVE-YEAR SALVAGE OF TREATED AND UNTREATED PATIENTS

CONDITION 5 YEARS AFTER TREATMENT	PATIENTS	
	NUMBER	PER CENT
Alive	94	44.5
Dead	117	55.5
Total	211	100.0

FIVE-YEAR SALVAGE BASED ON METHOD OF TREATMENT

1. *Hysterectomy*.—In our clinic the operation of choice has been radical pan-hysterectomy, with removal of both adnexa when this procedure is not contraindicated.

From Table VII it will be observed that 115 patients were treated by hysterectomy. In this group are included those patients in whom irradiation was either preoperatively or postoperatively combined with hysterectomy, since we feel that in the

time covered by this analysis irradiation as an adjunct to surgery was not a routine measure and that the group is too small from which to draw any positive conclusions. Moreover, it is likely that the irradiation was in most cases inadequate. Of the 115 patients treated by hysterectomy, 55 patients survived five years or longer, a salvage of 47.8 per cent. Panhysterectomy was performed in 80 cases and supravaginal hysterectomy in 35. The reason for incomplete operation was in most cases either inability to remove the cervix, due to fixation by the malignant process, or a failure to suspect the condition in cases in which the diagnosis was made by histologic examination. When we compare the salvage in the two types of hysterectomies, we see that the salvage favors the complete operation, the proportion being 53.7 per cent as compared to 34.3 per cent. In the years prior to the use of irradiation no further treatment could be instituted, whereas today radium can be applied to the cervical stump and roentgen ray therapy be employed, thus yielding a more favorable prognosis in those cases in which complete hysterectomy cannot be performed.

2. *Irradiation.*—Eighty-nine patients were treated by means of curettage and irradiation: Thirty-nine patients, 43.8 per cent, survived the five-year period. Although definite changes as regards the total dosage in the initial irradiation of fundal carcinoma have taken place in the last five years, the average dosage in this series was only 2,400 mg. hours. Today this amount of irradiation is considered

TABLE VII. FIVE-YEAR SALVAGE BY METHOD OF TREATMENT

TREATMENT	PATIENTS		
	NUMBER	ALIVE	PER CENT
Hysterectomy	115	55	47.8
Radium	89	39	43.8
Untreated	7	0	0
Total	211	94	44.5

inadequate, but even with this small dosage, it was still of distinct curative value in over 40 per cent of cases, nearly all of which were poor operative risks. This does not take into consideration prolongation of life in hopeless cases and the greater comfort which accrues. In comparing our results as to methods of treatment, the salvage is approximately the same in the group treated by hysterectomy as in those treated by irradiation alone, namely, 47.8 per cent and 43.8 per cent, respectively. In comparing the two methods of treatment it should be remembered that of the patients treated by hysterectomy, only 74.8 per cent were traced, whereas of those patients treated by irradiation, in general a more recent group, 92.1 per cent were traced. In comparing the salvage in the patients treated by *panhysterectomy*, whether alone, preceded by, or followed by irradiation to the salvage in the patients treated by radium alone, the salvage favors complete hysterectomy in the proportion of 53.7 per cent to 43.8 per cent. Although our figures as regards salvage do not vary unduly in the two methods of treatment, the procedure of choice is considered to be radical panhysterectomy in the operable cases, followed by deep roentgen ray therapy. In the advanced or inoperable cases of fundal carcinoma, or in those in whom some contraindication to a radical operation exists, irradiation is the method of choice. From our statistics, no conclusions as to the rôle of radium as a preliminary treatment to hysterectomy can be reached, because of the small dosage that has been employed.

Tables VIII, IX, and X show five-year salvage in five-year periods with the exception of the years 1900 to 1910 in the patients treated by hysterectomy, radium, and the combined five-year salvage on all patients who were treated.

TABLE VIII. FIVE-YEAR SALVAGE IN CASES TREATED BY HYSTERECTOMY

YEAR	PATIENTS		
	NUMBER	SALVAGE PER CENT	FOLLOWED PER CENT
1900-1910	15	20.0	60.0
1911-1915	19	36.8	68.4
1916-1920	25	52.0	80.0
1921-1925	37	59.4	78.4
1926-1930	19	52.6	78.9
Total	115	47.8	74.8

TABLE IX. FIVE-YEAR SALVAGE IN CASES TREATED BY RADIUM

YEAR	PATIENTS		
	NUMBER	SALVAGE PER CENT	FOLLOWED PER CENT
1900-1910	0	0.0	0.0
1911-1915	1	0.0	100.0
1916-1920	18	44.4	88.8
1921-1925	30	36.6	90.0
1926-1930	40	50.0	95.0
Total	89	43.8	92.1

TABLE X. COMBINED FIVE-YEAR SALVAGE ON ALL PATIENTS TREATED

YEAR	PATIENTS		
	NUMBER	SALVAGE PER CENT	FOLLOWED PER CENT
1900-1910	15	20.0	60.0
1911-1915	20	35.0	70.0
1916-1920	43	48.8	83.7
1921-1925	67	49.3	83.6
1926-1930	59	50.8	89.8
Total	204	46.1	82.3

CONCLUSIONS

1. Childbearing plays no part in the predisposition to fundal carcinoma

2. The chief symptoms are bleeding and discharge. Metrorrhagia was the first symptom noted in 80.5 per cent of the cases.

3. The average duration of symptoms was 17.9 months. If myomas and fundal carcinoma were associated, the average duration of symptoms was 21.8 months.

4. Only 43.8 per cent of patients sought treatment prior to one year after the onset of symptoms.

5. The preoperative diagnosis was positive in 67.9 per cent of cases, suspected in 16.6 per cent, and unsuspected in 15.5 per cent.

6. All uteri removed for what are believed to be benign lesions should be opened and the endometrial cavity inspected before the operation is completed.

7. Diagnostic curettage is the most certain method of detecting the presence of early fundal carcinoma and may be relied upon in practically all cases.

8. The association of myomas and fundal carcinoma occurred in 34.9 per cent of our cases.

9. Of 13 patients with involvement of the ovary treated five or more years ago, 6 survived the five-year period, and in 14 cases in which the parametrium was invaded, 3 survived the five-year period.

10. For uncomplicated cases, a radical panhysterectomy and bilateral salpingo-oophorectomy, followed by deep roentgen therapy, is the treatment of choice.

11. When curettage is performed in a suspected case, a minimum of 1,200 mg. hours of radium irradiation should be employed. If broken-up particles of carcinoma are left behind in the uterus, the irradiation tends to prevent dissemination, and if the case proves to be benign, bleeding is checked.

12. The five-year salvage in patients treated by hysterectomy was 47.8 per cent.

13. The five-year salvage in patients treated by radium alone was 43.8 per cent.

14. The operative mortality for the series was 3.4 per cent.

15. In the patients treated by hysterectomy, the operative mortality was 4.3 per cent, and in patients treated by radium, it was 2.2 per cent.

16. The absolute five-year salvage in the entire series was 44.5 per cent, and the relative five-year salvage was 46.1 per cent.

A CRITICAL STUDY OF THE LOW CERVICAL AND CLASSICAL CESAREAN SECTION OPERATIONS*

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THERE has been considerable controversy concerning the relative merits of the classical and the low cervical operations for cesarean section. Such a reaction is inevitable when a different technic is proposed for a procedure in which the standard operation is giving reasonably good results in the hands of well-trained surgeons.

The difference of opinion seems to arise from the fact that certain operators desirous of finding some way to minimize the inherent risk in cesarean section have adopted the newer operation and use it exclusively. Others, more conservative, either refuse to try the new procedure on the ground that it does not appeal to them as an improvement over the older operation, or else having tried it in a few cases, decide that it is not the operation of choice because of some technical difficulty which they may have encountered.

*Read before the Chicago Gynecological Society, March 20, 1936.

The diversity of opinion may be appreciated by the expression of several outstanding authorities.

Williams¹ felt that the classical operation was preferable in those cases in which the probability of intercurrent infection was slight; where this probability was great he preferred the low cervical operation. Where evidence of infection could be demonstrated clinically he preferred the Poro operation.

Bland² advocates the classical operation in all patients who can safely be placed in the category called "clean." The low cervical operation is advised in those who have been long in labor with membranes ruptured or have had vaginal examinations, or other manipulation.

DeLee,³ on the other hand, strongly favors the low cervical cesarean section. He claims that there is less hemorrhage, less ileus, less gastric dilatation and peritonitis, and that wound healing is better because the lower uterine segment following operation is at rest. He also claims that the maternal mortality of the low cervical operation is less than following the classical. These advantages would be quite significant if demonstrable. No proof is adduced however to support this contention.

Beck⁴ also favors the low cervical cesarean operation, claiming less danger because of limitation of the spill, the low position of the uterine wound tending to localize the infection in the pelvis in those cases in which infection develops. Less hemorrhage and distention and fewer adhesions. Again, however, these advantages are based on clinical impression, no proof is presented to support the contention.

I wish to point out several factors which may contribute to a false impression in evaluating the results obtained by the new operation.

The sponsors of the new procedure quote the results obtained in a given number of cases since its adoption. The apparent improvement in their results is attributed by them to the new procedure. No weight is given to the fact that they, after doing a considerable number of operations, using the old classical technique, are better prepared by that experience to do the next series of cases, no matter which technique is used.

As an operator grows in experience, so also there appears in his clinic a cooperation, attention to detail, and smoothness of execution by the resident and nursing staff and the anesthetists, all of which are important contributing factors in lessening the operative shock and reducing the operating time, which in turn inevitably reflects itself in improved operative results.

In some instances because of relative unfamiliarity with the new procedure, the old or classical technique is elected for the difficult cases. The low cervical operation is used only in those cases in which no technical difficulty is anticipated.

Not infrequently statistics from clinics are compared where the circumstances surrounding the operation are widely different.

Statistics of the present are unfairly compared with the statistics compiled years ago.

Results of trained obstetric surgeons are contrasted with those of general practitioners in a given community.

The conservative, on the other hand, will have nothing to do with the new procedure because the principles involved do not appeal to him. Or

he will give it up after a trial or two because of some difficulty encountered, or poor results. He has obtained good results, with the older procedure, low mortality and morbidity, and cannot see the advisability of changing to the new technique until its advantages are conclusively demonstrated.

How then are we to arrive at a reasonable estimation of the value of a new procedure, since we have to rely almost entirely on the published reports of men who have a more or less biased viewpoint, and whose published results cannot but reflect the same.

One rational method of settling such disputes is extremely simple and satisfactory, even though somewhat slow. If an operator will set himself to the task of alternating the two operations on the cases as they present themselves for operation, the results will speak for themselves as soon as a sufficient number of cases have been accumulated. The personal equation is thus reduced to the minimum.

Certain advantages are claimed by the sponsors of each operation.

The advocates of the low cervical operations claim for its superiority on the ground that:

1. Wound healing is better because the lower uterine segment is passive during the puerperium, and therefore better healing is promoted.
2. There is therefore less likely to be a rupture of the uterus in subsequent pregnancies.
3. Infection if it occurs and penetrates the uterine wound will be limited to the extraperitoneal space behind the bladder, for a time at least, before producing infection of the general peritoneal cavity.
4. The operation is usually completed without the intestines coming into view, reducing thereby the danger of peritoneal contamination and ileus.
5. There is less postoperative discomfort, vomiting, and ileus following the low cervical operation.
6. There is less danger of adhesions forming between the uterine and abdominal wound.

The advocates of the classical operation say:

1. That there is no evidence that the wound healing takes place under any more quiet conditions in the low cervical than in the classical operation.
2. That the thicker the surfaces of uterine muscle that are approximated the better the scar.
3. That there is less danger therefore of rupture of uterine scar in subsequent pregnancies.
4. That when properly done in noninfected cases, there is very little danger of infection coming through the uterine wound.
5. That the low cervical section is more dangerous, time-consuming, and technically more difficult.
6. That there is more danger from hemorrhage when the placenta is in the lower uterine segment.
7. That there is no reason for exposure of the bowel or more contamination of the peritoneal cavity in the classical operation.
8. That there is less danger of bladder injury and cystitis.

It was in the hope of throwing some light on these questions that this series of operations was undertaken.

I have, in the last ten years, collected a series of cesarean sections personally done in the same clinic, under identical conditions. As nearly as possible the cases were alternated. There was no deviation in favor of either operation because of potential infection, placenta previa, serious toxemia, or other complications. The results, therefore, although the series is not large, should speak definitely as far as they go for the relative merits of the two operations.

In order to place clearly before you how these patients were treated, I shall give a brief outline of the technic of both operations as done in my clinic.

In the classical operation the following steps were carried out:

1. The patient is placed in the Trendelenburg position after preparation of skin with iodine and alcohol as for ordinary laparotomy.

2. A midline incision is made from just above the pubes almost to the umbilicus.

3. The uterus is rotated if necessary to bring the midline of the uterus into the center of the abdominal wound.

4. An incision is made in the anterior uterine wall beginning just above the vesicovaginal peritoneal fold and extending upward about 12 cm.

5. The baby is delivered by grasping a foot and extracting by the breech.

6. Pituitrin 1 c.c. obstetric is injected into the uterus.

7. The edges of the uterine wound are grasped by Allison forceps on each side and the placenta and membranes are delivered manually.

8. Ergotol one ampule is given hypodermically as soon as the placenta is delivered.

9. The uterine wall is repaired, with the uterus in the abdomen as a rule, with four layers of chromic catgut as follows: The first row of sutures is a continuous double No. 2 chromic catgut suture, starting near the pubic end of the wound and taking about half the thickness of the uterine wall, extending down to but not through the mucosa of the uterus. When this stitch is tied at the upper end of the wound the uterine cavity is effectively closed off. The next stitch beginning at the lower end of the wound and continuing to the upper end is made by inserting the needle just under the serosa and carrying it down to interdigitate with the preceding row of stitches. The next layer approximates the edges of the serosa and interdigitates with the second layer. The final layer is the peritonealizing layer. It is done with fine catgut. The loose vesicouterine peritoneum on each side of the lower end of the wound is sewed over the wound from below upward. It will be found that in most cases about half of the wound can be covered by this loose peritoneum. From here to the upper end of the incision, the peritoneum and a small bit of the muscle on each side of the wound are caught in each stitch which when drawn tight buries the scar. The free blood and clots are removed from the abdominal cavity, and the abdominal wound is closed in layers.

The technic for the low cervical operation was as follows:

1. Position, preparation, and abdominal wall incision are the same as in the classical operation.

2. The loose peritoneum between bladder and lower uterine segment is raised and cut transversely from one broad ligament to the other. The lower leaf is pushed down with the bladder off the lower uterine segment.

3. The latter is incised in the midline, care being taken to avoid cutting the baby, since the lower uterine segment is very thin. The fetal head is then rotated so that the occiput points into the wound, forceps are applied and the baby is gently extracted.

4. Pituitrin and ergot are given as before and the placenta is either expressed or delivered manually.

5. The edges of the incision are about 2 mm. thick, except at the upper angle of the wound where invariably the upper uterine segment is invaded in all cases that have not been in labor. The edges are grasped by Allison forceps and closed by a running No. 2 chromic catgut suture. Often a second continuous stitch can be placed in the uterine muscle. Next a thin layer of fascia between the bladder and uterus is closed over the uterine wound. The transverse incision in the peritoneum is sewed over the wound with No. 1 plain catgut. In case infection is strongly suspected, I push the bladder off the anterior vaginal wall, incise the latter and put a drain into the vagina. The upper part of the drain lies on the scar in the uterine wall. Any seepage from the uterine cavity is thus led directly into the vagina. The drain is removed in forty-eight hours if no infection occurs. The peritoneal cavity is then freed of blood and clots and the abdomen closed in layers.

In estimating the results in the two series of cases several factors were thought to be of importance to determine the comparative morbidity, reaction, and distress. The age and parity were noted because obviously a great difference either way in either group might have a significant bearing. The indication for operation was also noted because a patient with placenta previa or severe toxemia might be a poorer operative risk than one with a contracted pelvis. For the same reason the cases complicated by syphilis were also noted as well as all those having evidence of associated nephritic or preeclamptic toxemia.

The operating time was observed for two reasons; because of the bearing that this might have on shock, hemorrhage, and infection, and to determine to some extent thereby the relative technical difficulty of the two operations. For the same reasons the type of anesthesia was recorded. Vomiting and partial ileus were taken as a rough measure of the peritoneal reaction following the invasion of the peritoneal cavity. The number of times vomiting occurred postoperatively and the number of enemas necessary to produce flatus and relieve distention were taken as the measure of the ileus.

The highest temperature on the days in which the temperature reached 100° or more postoperatively was recorded and supplemented by the report of wound infection and the number of days the patient remained in the hospital after operation was taken as the index of morbidity.

The amount of postoperative discomfort and pain was roughly measured by the amount of morphine administered postoperatively. Our routine for postoperative treatment is a quarter of a grain of morphine if there is discomfort a few hours after operation and a sixth of a grain every four hours as necessary subsequently.

In addition, we noted the number of catheterizations necessary postoperatively because of the general impression that the low cervical operation is more likely to give rise to bladder irritation and complications.

We also noted whether or not the membranes were intact or ruptured before operation, because of the obvious bearing on potential infection.

The weight and length of the baby were also recorded together with the condition at birth and the final outcome.

The results obtained from the study of these cases are interesting for several reasons. The average age was found to be 24 in the low cervical and 25.7 in the classical group; there were 37 multiparas and 20 primiparas in the low cervical cesarean section group, and 35 multiparas and 22 primiparas in the classical group.

The indications for operation are seen in Table I. It will be noted that there was no great preponderance of pathologic cases in either group.

TABLE I. CLINICAL CASES

		57 CASES LOW CERVICAL	57 CASES CLASSICAL
<i>Indications:</i>	Placenta previa	10	3
	Premature detachment	8	11
	Heart lesions	3	6
	Contracted pelvis	15	17
	Eclampsogenic toxemia	8	6
	Miscellaneous	7	3
	Previous cesarean	12	15
<i>Age:</i>		24	25.7
<i>Para:</i>	Primipara	20	22
	Multipara	37	35
<i>Wassermann:</i>		5	2
<i>Toxemias:</i>	Preeclamptic	12	11
	Thyroid	0	2
<i>Operating Time:</i>		43 min.	44.4 min.
<i>Anesthesia:</i>	Sterilizations	13	16
	General	53	46
	Local	4	11

TABLE II. CLINICAL CASES

	57 CASES LOW CERVICAL	57 CASES CLASSICAL
Vomiting total number	19	28
Ileus partial	4	8
Temperature above 100°		
Average days per case	3	4.37
Days in hospital		
Average postoperative	15	16.4
Average amount of morphine		
Postoperatively per case	$\frac{9}{12}$ gr.	$\frac{7}{12}$ gr.
Total number of catheterizations	16	33

The average operating time was forty-three minutes in the low cervical series and forty-four and four-tenths minutes in the classical series. This result may have been influenced by the fact that 11 of the classical cases were done under local anesthesia, which always slows up the operation, to 4 of the low cervical, and, also, to the fact that one of the classical cases had a ventral hernia which was repaired after sewing up the uterus. Other factors which would add to the operating time such as

sterilization by exsection of the uterine end of the tube and adhesions due to previous cesarean sections were about equal in the two series.

I was somewhat surprised by the result since the commonly accepted view is that the low cervical operation is technically more difficult and more time-consuming. From my experience I should say that the operation is not appreciably more difficult and that there is practically no difference in the operating time if the conditions for the operation are the same.

The anesthesia most used in both series was ethylene, to which was added a small amount of ether, just as the abdomen was opened to secure better relaxation. In the classical group 11 had local anesthesia, 1 per cent novocaine with no preliminary morphine and scopolamine, because of the danger of depressing the respiratory center of the baby. Only 4 of the low cervical group were done under local anesthesia. There was no special reason for the discrepancy in this respect in the two groups since technically the operation under local anesthesia is not difficult. A small number of each series had ether only and a few had nitrous oxide only.

As an indication of the postoperative shock, ileus and peritoneal reaction, we observed the number of times the patients in each series vomited postoperatively, and, also, the cases that had to have repeated enemas to relieve the gaseous distention postoperatively.

In the classical group, emesis occurred 28 times, while in the low cervical group it occurred 19 times. In the classical group, 8 cases had sufficient obstipation to be classified as mild ileus, while 4 of the low cervical cases were so classified.

In the classical group the average postoperative days in which the temperature reached 100 or more was 4.37. In the low cervical group the number of temperature days was 3.

The number of postoperative hospital days for the classical group was 16.4 as opposed to 15 for the low cervical group.

Wound infection occurred in 4 of the classical cases while only 2 of the low cervical cases had wound infection.

As an index of the postoperative discomfort, it is interesting to see that the average amount of morphine given in the classical cases was $\frac{7}{12}$ of a grain, while the average for the low cervical cases was $\frac{6}{12}$ of a grain. The difference is hardly appreciable.

The membranes were ruptured for a short time before operation in 4 patients in the classical series, while in the low cervical series the membranes had ruptured in 3 patients.

As a rough measure of functional bladder disturbance following the two operations, the number of postoperative catheterizations was taken. It was found that catheterization was necessary 33 times in the classical

series, and only 16 times in the low cervical group. The often quoted danger of bladder traumatization in the low cervical operation seems to be theoretical rather than real according to these figures.

There was one death in this series which occurred in the classical group. A brief description of the case is as follows:

A para x, twenty-six weeks pregnant, entered the hospital with a diagnosis of severe nephritic toxemia. Because of the prematurity of the baby, an attempt was made to carry the patient along until viability. This was carried out for twenty-six days in spite of severe symptoms which did not yield in medical management. Finally when the baby seemed to be on the borderline of viability, we did a cesarean section under local anesthesia. This was accomplished without difficulty in forty-seven minutes, including sterilization. The patient developed a peritonitis and bronchitis and died on the fourth day. The anatomic diagnosis at the postmortem examination was as follows:

Generalized peritonitis, extreme fatty degeneration of the liver, early arteriosclerosis and arteriolosclerosis of the kidneys with marked fatty degeneration, early bronchopneumonia of the right upper lobe, marked congestion of both lungs, hypertrophy of the thyroid, and puerperal uterus with recent ulcerative colitis.

I do not feel that the disastrous outcome in this case can be attributed solely to the operative procedure. I should rather attribute it to faulty judgment on my part in trying to prolong gestation to viability of the baby in the face of a toxemia not responding to medical management. The decision to do a cesarean section instead of induction of labor was based on the fact that the fetal heart tones suddenly became very irregular, varying from 80 to 160 beats per minute. The uterus at postmortem was a normal puerperal uterus so that the peritonitis was not due to faulty healing of the uterine wound.

In addition to the above described series of cases done in my clinic, I have operated upon 49 patients at various private hospitals in Chicago. Twenty-three classical and 26 low cervical operations were done. The preoperative and operative factors are shown in Table III and the results are shown in Table IV.

In this series the results are practically the same as in the previous series. Age, parity, and anesthesia were practically the same for each group. The patients in the low cervical series were in the hospital one day less but ran a slightly higher temperature, and showed much more vomiting, slightly less ileus and less bladder irritability. There was slightly more pain since $\frac{1}{6}$ gr. more of morphine was used in these cases. The operating time was about equal which is the more significant since assistants were different in most of the cases. There was no mortality in either group. The total morbidity in this series seems to be slightly less in the classical group.

It would seem therefore that the same conclusions, namely, that if done by the same operator there is no appreciable difference in the results obtained by the two operations, whether done on clinical patients with the same type of assistance in the same hospital or whether done in different institutions, with different assistants on private patients.

TABLE III. PRIVATE CASES

		26 CASES LOW CERVICAL	23 CASES CLASSICAL
<i>Indications:</i>	Placenta previa	1	0
	Premature detachment	2	1
	Heart lesions	0	0
	Contracted pelvis	9	3
	Eclamptogenic toxemia	7	7
	Miscellaneous	2	9
	Previous cesarean sections	3	3
<i>Age:</i>		29.8	30.9
<i>Para:</i>	Primipara	15	10
	Multipara	11	13
<i>Wassermann:</i>		0	0
<i>Toxemias:</i>	Preeclamptic	7	7
<i>Operating Time:</i>		43.6	43
	Sterilizations	1	0
<i>Anesthesia:</i>	General	23	21
	Local	3	2

TABLE IV. PRIVATE CASES

		26 CASES LOW CERVICAL	23 CASES CLASSICAL
	Vomiting total number	15	5
	Ileus partial	9	11
	Temperature above 100°		
	Average days per case	3.2	3
	Days in hospital		
	Average postoperative	14.2	15.4
	Average amount of morphine		
	Postoperatively per case	$\frac{9}{12}$ gr.	$\frac{8}{12}$
	Total number of catheterizations	16	21

From the foregoing it will be seen that there is no significant difference in the results obtained in the two series. The clinical group showed slightly more morbidity in the classical series. The private group showed a little more morbidity in the low cervical series. In both groups the bladder irritability was less marked in the low cervical and was insignificant in both groups. An indwelling catheter was not used in any of these cases. None of them was complicated by postoperative pyelitis or serious cystitis. Since in the larger group of clinical cases there was a slight apparent increase in morbidity, the burden of proof seems to lie with those who claim the classical operation is the operation of choice. Since, however, the difference between the results is so small in my hands, I feel justified in continuing the experiment I have started until I have accumulated more evidence. It would be desirable for other clinics interested in the subject to adopt this method so that comparable statistics might be compiled.

CONCLUSIONS

1. As regards morbidity and mortality in the series, there appears to be a slight difference in favor of the low cervical operation.

2. As regards postoperative vomiting, ileus and temperature days, hospital days and wound infection, there appears also to be a corresponding slight difference.

3. There seems to be no difference in the postoperative discomfort.

4. There seemed to be less bladder dysfunction after the low cervical than after the classical operation.

5. There is no appreciable difference in the technical difficulty as measured by the operating time.

6. The results obtained by the low cervical operation are hardly so superior to those following the classical operation as to justify the extravagant praise of some of its sponsors.

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30 NORTH MICHIGAN BOULEVARD

DISCUSSION

DR. WILLIAM C. DANFORTH.—For many years we did the classical operation as a routine procedure, reserving the low cervical for women who had gone into labor, or whose membranes had ruptured, or when a test of labor had been decided upon. Our impression is the same as Dr. Falls', but we feel the superiority of the low cervical operation is more marked. I do not know whether he alluded to the management of relative contraction in which a test of labor is used. It seems to me that in those cases particularly, the superiority of the newer technic is quite definite. It has been so in our experience. Formerly when we did classical section upon a woman in labor or one whose membranes had ruptured, the convalescence was very definitely stormy. Our convalescences in low cervical sections have been quite definitely better. Since 1922, through 1935 and not counting the cases in 1936, we have done 341 low cervical sections. In the same period the classical section was done only 60 times. Some years ago I looked up our mortality with classical section, and it was 4 per cent. I think the large mortality was due in part to the toxemia or eclampsia from which the women suffered, because when I first went into practice we were delivering all patients with eclampsia by one or the other operative means. The mortality for the patients who had 341 sections since 1922 is 0.87 per cent. In almost 50 per cent a test of labor had been carried out. It seems to me that the low cervical operation is definitely superior to the classical not only from the standpoint of mortality, but also from the standpoint of morbidity, as recoveries have been smoother with the new type of operation than with the older.

As to the low cervical section in placenta previa, we formerly preferred the classical. In late years we have done the low cervical on almost all patients with placenta previa. I think in some cases of central placenta previa the older operation is still preferable, but the risk of the new operation in placenta previa is no greater than in the old. Bleeding sinuses may be stitched over if needed, and one can pack more easily than with the classical. I agree with Dr. Falls except that we believe the superiority of the new operation is greater than his experience has shown.

DR. RUDOLPH W. HOLMES.—My cesarean experience covers a period of over thirty-six years; during that time I have seen the furor aroused by the advocates of one variant in technique to another: in this period the sites for the diverse uterine incisions, if made continuous, would sagittally bisect the uterus from the cervix anteriorly to the same structure posteriorly: and numerous coronal incisions have been recommended. I have never been swayed by the enthusiasms of proponents for one or the other. Three factors influence cesarean section mortality: the first, and most fundamentally important element, is the indication. The range covers the operation for eclampsia where the fatality is the highest, and is lowest, occurs in contracted pelvis, where the patient is otherwise perfectly well, or where the unjustifiable operation is performed as a "matter of convenience."

The second factor is the environment in which the operation is done: hospitals which have perfectness of cooperation of the personnel, and operating room equipment complete in every detail, will have a relatively low mortality, whereas, where the converse holds true the mortality rate necessarily will be high.

The third factor is the operator: he who carefully "selects" patients who will be safe surgical risks will have a low mortality—but, if patients are selected for operation, and then the operation is rejected on account of extraneous circumstances, and ultimately have a spontaneous termination of labor, it is *prima facie* evidence that the primary placing of the indication for cesarean was spurious. The man who meticulously carefully adheres to the tenets of conservative obstetric principles and operates on pressing indications will necessarily have a considerable mortality.

In 1922 I reported 92 cesarean sections before the American Gynecological Society, among which were 6 maternal deaths (2 were eclamptic patients with pelvic contraction which dictated the operation) and 8 fetal deaths, of which 2 were still born; 2 were hydrocephalic, the operation being indicated for gross pelvic deformity; and 4 died within fifteen days from nonobstetric causes.

After reading the paper, one of the outstanding proponents of the low cervical cesarean section, which then was newly revived, told me I would not have had the high thermal reactions if I had performed the low cervical operations—an operation practically unknown during the period in which most of my operations were performed!

In my paper the operations were grouped into those patients not in labor, those in labor, and those with membranes ruptured; the high and low temperatures for ten days were recorded; the averages for each group were recorded and charted. The exponent of the new cervical section had recently reported his series with the temperature charts. I took his 7 operations which had been longest in labor with membranes ruptured, and the same number of mine. In his series the duration of ruptured membranes ranged from thirty-six to seventy-two hours, an average being fifty-one hours while mine ranged from twenty-four to eighty-four hours, average fifty-two hours: the average duration of labor in his patients was forty hours, while mine was forty-six hours. The high and low temperatures of the several groups were averaged for the ten days, and a chart made which I show you. You will note that operative results, as far as the temperature is concerned, do not compare with mine. You must remember that my series covers the period from the time when an Esmarch constriction about the cervix was deemed essential, and the period when eventration of the uterus was considered the wise expedient. But temperature alone is not the sole criterion: Dr. Falls has presented indisputable evidence that the type of operation is relatively immaterial and irrelevant—success is more determined by the given operator and his environment than any and all other influences. Enthusiasm for a new operation dims an operator's perspective—and his deductions are prone to be fallacious; too, a comparison of results of recent cervical sections with past experiences with classics is grossly faulty.

I have in preparation a survey of cesarean section in 420 American hospitals. It is too early to offer much advanced information, but I would cite a few facts.

In one hospital there were 22 classic operations with a mortality of 4.5 per cent, while in 7 cervicals the mortality was 14 per cent. In another hospital 12 classics had no mortality, while in 15 cervicals the rate was 6.6 per cent. In still another hospital the classic rate was 4.9 against 9 per cent for cervical. One hospital had 72 classics and 70 cervicals without maternal mortality.

Dr. Falls has definitely proved his contention that the place of the incision is inconsequential; the crux of the situation lies in the operator himself.

DR. RALPH A. REIS.—I should like to ask Dr. Falls if he now advocates a low cervical cesarean in contradistinction to the classical type? Also, has he found that one of the advantages of the low cervical type is the lack of postoperative adhesions involving the omentum, uterus, and bowel? We have found at Michael Reese Hospital that when we do low cervical section, we have had less adhesions than following the classical type of operation. Dr. Falls in his series had a large number of repeat cesarean sections, and I wonder if he could clear up that point. It would seem that with the bladder covering the lower segment there should be less adhesions following the low cervical operation, and I should like to know whether Dr. Falls' experience has been the same as ours.

DR. FALLS (closing).—Dr. Danforth's point about doing the low cervical operation after the test of labor is well taken. As a result of this study I believe in such cases the low cervical operation is indicated. In our series, however, no deviation in favor of the low cervical operation was practiced in such cases. One should be careful in interpretation of clinical impressions as mentioned by Dr. Danforth. The actual figures gathered in this study upset several of my previous impressions.

The cesarean section as practiced in this series for eclampsia and eclamptogenic toxemia resulted in one death in 28 cases, a mortality of 3.5 per cent.

In placenta previa, I do not think it makes any difference whether one does a low cervical or a classical operation. There is a possible advantage to being able to see a bleeding point while doing a low cervical, but we have never sutured a bleeding point in a low cervical, though we have done more of these operations than classics in placenta previa. After taking out the placenta, if there is bleeding, we pack the lower uterine segment and sew over the pack. Theoretically and practically there is no question but that one could put in a stitch. It is rarely necessary.

The point stressed by Dr. Holmes that the individual operator may change the result in comparing these operations, is very important. That is why I did every operation myself from start to finish. All fever we ascribed to inflammation and not to thermal reaction, which as Dr. Holmes said is "quibbling." As far as postoperative adhesions are concerned, we have opened the abdomen subsequently in several patients and we did not see very many adhesions with the classical operation, done as we do it. I think postoperative adhesions come from one thing, that is peritonitis. Evidence that there is less peritonitis in the low cervical operation than in the classical operation is lacking in this series.

Harrisson, E. H.: The Eynesbury Quadruplets, Brit. M. J. 2: 1207, 1935.

An account of the delivery of these quadruplets is given. Nothing is unusual in the management of the case. The placenta is of interest. It appears that three ova were fertilized, and the first two infants were bi-amniotic twins from one ovum. It appears then that one, two, three, or four ova may be involved in the production of quadruple pregnancy.

F. L. ADAIR AND S. A. PEARL.

✓ANALYTICAL STUDY OF 347 CONSECUTIVE CESAREAN SECTIONS

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CESAREAN section is accompanied by a greater morbidity and mortality than uncomplicated simple laparotomy. It would appear from a study of the situation that the technical surgery involved is far less important than a well-organized effort to intelligently interpret and evaluate the attendant general and obstetric status of the patient. Mature deliberate obstetric judgment plays a much more important rôle than the equally necessary obstetric operation. Improvements in technic and a more comprehensive understanding of the conditions under which the abdominal route may be preferred have substantially reduced the initial risk. In weighing the hazards of fetal injury or extensive maternal damage, suprapubic delivery is often chosen as a solution of the problem.

INDICATIONS FOR OPERATION

We have adopted the classification of indications as outlined by Gordon,¹ with such modifications as are explained under the proper headings. The plan of grouping has been:

1. Cases of contracted pelvis.
2. Cases of eclampsia and other toxemias of pregnancy.
3. Cases of antepartum hemorrhage (placenta previa and accidental hemorrhage).
4. Other conditions.

The most frequent indication for section was contracted pelvis, totaling 206 cases or 59.3 per cent. In the second group were 7 cases of eclampsia and 14 cases of preeclampsia. The third group was composed of 23 cases of placenta previa and 9 cases of ablatio placentae, 4 total and 5 partial. Among other conditions were listed the following:

Cardiac disease	14
Disproportion	24
Cervical dystocia	19
Multiple fibroids	5
Breech	2
Persistent occipitoposterior	3
Habitual stillbirth	2

and 1 each of the following:

Interposed uterus	Psychosis
Ruptured uterus	Previous myomectomy
Paraplegia following encephalitis	Previous poliomyelitis
Previous third degree laceration	Hypertension
Torsion of uterus	Hemiplegia plus hypertension
Ventral fixation	Pulmonary tuberculosis with unengaged head
Hemiplegia	Kyphotic pelvis in an elderly primipara
Transverse presentation	

Three hundred and forty-seven cesarean sections were done by 20 surgeons, representing 1.56 per cent of 23,031 total deliveries during a thirteen-year period up to December, 1935. Of these, 163 were of the classical type. Our feeling has been that there is still a definite field for the classical operation and where the results have been bad, investigation has usually revealed the use of faulty judgment in the selection of the case; 126 were of the low two-flap Beck operation; 47 were of the low transverse cervical operation popularized by Phaneuf. There were 6 classical cesarean sections with extraperitonealization of the uterine incision; there were 3 cesarean sections with hysterectomies of which two were done for fibroids plus pregnancy and the third for a neglected case following a previous interposition operation. During the past year the low transverse cesarean section has been adopted by some members of the staff, and my conclusion is in agreement with the claims of Phaneuf.² It had been noted that when the low cervical longitudinal uterine incision was employed it was sometimes found necessary to extend it superiorly into the body of the uterus when delivering a large fetal head. This resulted in a failure to secure all the advantages that accrue in keeping the uterine incision below the isthmus. Also, when the operation was performed before term, the lower segment was found to be too short to permit the easy access of the fetus. Finally, less separation of the bladder from the cervix was found necessary.

The classic cesarean section with extraperitonealization of the uterine incision, in which the parietal peritoneum is sutured around the uterine incision, was done in 6 cases by one member of the staff with uniformly bad results. High morbidity, marked abdominal distention, considerable vomiting and scant foul lochia were predominant. There appeared to be a restraining interference with the normal contraction and retraction of the uterus with resulting delayed involution of the latter.

1. *The contracted pelvis group* included 55 cases of absolute contraction in which the indication was obvious and the delivery by cesarean section, either elective or following a short trial labor. The larger proportion were border-line contractions which necessitated the most deliberate obstetric judgment in their management. Many of these patients had entered the hospital with membranes ruptured; in others the membranes ruptured soon after admission. Most of these women developed poor ineffectual pains, usually accompanied by a maladjustment of the presenting part, and a discouragingly slow cervical dilatation. The crucial decision has been to determine where the margin of safety ends beyond which is the specter of an exhausted mother with diminished resistance to hemorrhage and infection, and a badly jeopardized baby. The recent epochal work of Caldwell and Moloy³ and Thoms⁴ in cephalopelvic relationship gives promise of more precise appraisal of cases of disproportion without recourse to a dangerously long trial test of labor. This group includes those with a previous obstetric history of prolonged labor and difficult instrument delivery, resulting in forbidding maternal and fetal damage. There were 41 resectioned cases, of which 39 were done for cephalopelvic disproportion; one for paraplegia, and one for recurrent placenta previa. Thirteen of this group were sterilized.

2. In the preeclampsia series (second group), the abdominal route has been referred for those severe preeclamptic patients who fail to respond to intensive well-directed therapy and become progressively worse. In cases where convulsions have already occurred, we have followed the accepted teaching that cesarean section is contraindicated and belongs in the same category with accouchement forcé. The occasional exception has been prompted by the feeling that "cesarean operation has a distinct though limited place and in cases where delivery by vaginal route offers great difficulty and where no improvement in the toxic condition is observed, after a reasonable application of sedative and eliminative measures, cesarean section with local anesthesia offers the best hope for a successful outcome" (Schulman).⁵

Third Group.—In both the primipara and multipara near term with moderate or profuse bleeding and with an undilated cervix, our present preference is delivery by cesarean section irrespective of the type of placenta previa.

Ablatio Placentae.—Cesarean section has been resorted to only in selected cases presenting signs of acute hemorrhage, either of the concealed or the frank variety, with an undilated cervix. In both of the foregoing groups, transfusion before operation has been a routine measure.

Fourth Group.—We have felt that most cardiac patients can be delivered safely from below. Nature often appears very kind to those so afflicted, and the ease of their delivery very often furnishes an agreeable surprise. In selected instances most of which have been cases of mitral stenosis, occurring in primiparas with a previous history of decompensation, the condition has been considered sufficiently serious to warrant abdominal delivery. This has applied particularly to those patients whose cardiac condition would be unlikely to tolerate safely the second stage expulsive efforts. This includes both the immediate risk as well as permanent residual additional pathology to an already damaged heart. The majority of these patients were sterilized, the former being a contributing indication for operation.

Interposed Uterus.—This rather unusual case is reported in detail. Case of multipara, forty-one years of age, full term, with history of previous uterine interposition done at another institution two years before, without sterilization. Admitted after three days of active labor at home under care of midwife; membranes ruptured four days; innumerable vaginal examinations. Temperature on admission 102°, pulse 140, spastic uterus, marked thyrotoxicosis; cervical stump barely admitting finger tip. Cesarean section and hysterectomy, recovery.

TYPE OF ANESTHESIA

One hundred and ninety-five patients had spinal anesthesia alone with one anesthesia death, which occurred before operation was begun; 123 patients were given ether and 8 cases induction gas followed by ether; 20 were done under local infiltration and 1 under sacral anesthesia.

Coincidental operations included 15 sterilizations and 1 myomectomy.

CONDITIONS AFFECTING MORBIDITY AND MORTALITY

A study of Table I reveals an increase in the morbidity rate in direct proportion to the time interval between the operation and the onset of labor plus ruptured membranes as shown so well in the survey of C. A. Gordon. The safe interval appears to be six hours after rupture of membranes or after the onset of labor. Following this there is an uncontrollable steady rise in the morbidity rate. It is likewise

apparent that the preoperative vaginal examinations must be reduced to the minimum if satisfactory morbidity standards are to be obtained. The standard taken for morbidity was a rise in temperature of 100.4° on any two successive days after the first day. Table II shows the causes when determined.

TABLE I. CONDITION AFFECTING MORBIDITY AND MORTALITY⁶

1. <i>Membranes ruptured</i>					
HOURS	TOTAL	MORBID	PER CENT	FATAL	PER CENT
0-12	259	50	19.1	10	3.8
12-24	40	11	27.5	2	5.2
24-48	22	9	40.9	2	9.09
48 or more	9	5	55.5	2	22.2
Not determined	17	5	29.4		

2. <i>Vaginal examinations</i>				
NUMBER OF EXAMINATIONS	TOTAL CASES	MORBID	MORBIDITY PER CENT	FATAL
One	43	15	34.8	1
Two	4	2	50.0	2
Three	4	2	50.0	0

3. <i>Hours in labor</i>				
HOURS	CASES	MORBID	MORBIDITY PER CENT	FATAL
0-12	173	19	10.9	10
12-24	67	21	31.3	3
24-48	84	31	36.9	2
48 or over	23	9	39.1	1

TABLE II. CAUSES OF MORBIDITY

Wound infection	19	Pyelonephritis	1
Lochia metra	19	Pneumonia	1
Thrombophlebitis (Saphenous)	2	Pulmonary infarct	1
Pyometra	1	Pelvic abscess	2
Parotitis	1	Pyelitis	4
Sapremia	14	Evisceration and pneumonia	1
Parametritis	6	Undetermined	8

Total number of cases with morbidity, 80 or 22.9 per cent.

CAUSES OF MATERNAL MORTALITY

There were 16 maternal deaths in this series of 347 cases, or 4.61 per cent. The causes were as follows:

Spinal anesthesia	1	Perforated peptic ulcer	1
Ruptured uterus	1	Pneumonia	3
Placenta previa	1	Pulmonary infarct	1
Peritonitis	4	Ablatio placenta	1
Sepsis streptococcemia	1	Nephritis uremia	1
Psychosis	1		

Of the foregoing, 3 cases, namely, the spontaneous rupture of the uterus, the perforated peptic ulcer, and the psychosis, are due to extraneous causes. Deducting these three gives us a corrected mortality of 3.74 per cent.

FETAL MORTALITY

STILLBORN	16 OR 4.61%
1. Premature separation of the placenta	6
2. Porro performed with fetus in utero	1
3. Mother died of spinal anesthesia: fetus left in utero	1
4. Placenta previa	4
5. Atelectasis	2
6. Toxemia	1
7. Ruptured uterus	1

Of the aforementioned, all six babies in the premature separation group were dead before operation. Eliminating these together with the two babies left in utero and the ruptured uterus case gives a corrected mortality of 2.01 per cent.

NEONATAL

1. Hydrocephalus	1
2. Heart anomaly	1
3. Toxemia	2
4. Esophageal stricture	1
5. Cerebral hemorrhage	1
6. Prematurity	1
7. Placenta previa	1

In this group eliminating the hydrocephalus, heart anomaly, esophageal stricture, and prematurity, gives a corrected mortality of 1.15 per cent.

TABLE III. MORTALITY AND MORBIDITY ACCORDING TO TYPE OF SECTION

METHOD	CASES	MATERNAL MORBIDITY	PER CENT	MATERNAL MORTALITY	PER CENT	FETAL MORTALITY	PER CENT
Classic	163	35	21.4	8	4.9	12	
Low cervical two-flap	126	34	26.9	7	5.5	3	2.4
Low cervical transverse	47	11	23.4	1	2.1	0	0.0
Classic with extra-peritonealization of the uterine incision	6	5	83.3	0	0.0	0	0.0

MORTALITY

Anesthesia.—Patient, aged thirty-two years, para i, admitted after thirteen hours in labor. Membranes intact; no engagement of head. Cervix three fingers dilated. Fetal heart was good. Cesarean section attempted under spinal anesthesia. As abdomen was opened, patient died, due to respiratory failure. Postmortem examination revealed no cause of death except that due to respiratory failure attributable to the spinal anesthesia.

Ruptured Uterus.—The patient was a forty-four-year-old para ix, who had a vertex presentation; she had had ten hours of moderate labor pains and was three fingers dilated. For no apparent reason she suddenly became pulseless and went into extreme shock. The abdomen was rigid. No pituitary extract had been given. An immediate laparotomy revealed a rupture of the uterus at the cervicovaginal junction extending into the broad ligament. She died on the operating table.

Placenta Previa.—Primipara, aged twenty-four years, full term, admitted with a history of sudden profuse painless hemorrhage; pulseless. Not in labor, unpre-

pared closed cervix, diagnosis made of placenta previa, classic cesarean section performed. Placenta found covering the cervical os and lower anterior uterine wall. Patient transfused during operation. In spite of intravenous pituitrin and uterine and vaginal gauze packing, patient continued to bleed. General condition poor. Vaginal packing became blood soaked, was removed and replaced. Intravenous 5 per cent glucose with saline started; adrenalin and caffeine sodium benzoate given as patient appeared exsanguinated. Patient died two hours later in spite of emergency treatment.

Peritonitis.—Primipara, aged nineteen years, admitted after six hours in labor. Membranes ruptured twenty-six hours. After labor of nineteen hours, two fingers dilated; cervix thick, breech presentation, not engaged; two-flap cesarean section performed. Day following operation temperature 103°. Marked abdominal distention. Patient died on the fifth day postoperative with symptoms of peritonitis.

Peritonitis.—Primipara, aged thirty-one years, admitted after eighteen hours in labor; with a justominor pelvis, and the fetus in a transverse presentation. No vaginal examinations done. Membranes ruptured two hours before operation. Classical cesarean section performed. Within twenty-four hours after operation her temperature rose to 103°, and thereafter gradually climbed to 107° on the fifth day, when she died. Postmortem inspection showed evidence of peritonitis (generalized).

Peritonitis.—Primipara, aged twenty-five years, admitted in labor with history of albuminuria and hypertension of two months' duration with generalized edema. After twelve hours of labor, no engagement; membranes intact. Classic cesarean section performed. On third day postoperative, marked abdominal distention. On exploration of wound, found separated with knuckle of gut caught in wound. Intestine replaced and abdominal wall resutured. On twelfth day postoperative, patient's condition poor; taken to operating room, wound reopened and abdomen explored. Uterine incision found gaping and several perforations of small intestine present. Evidence of general peritonitis. Patient received transfusion but died five hours after second operation. In retrospect it would appear that both these patients should have had two-flap extraperitoneal cesarean sections.

Peritonitis.—Multipara, para ii, aged thirty years. Two previous normal deliveries; in labor sixteen hours; membranes ruptured for five hours, position R. O. A.; cervix 2½ fingers dilated, head floating. Low two-flap cesarean section performed. Patient died on seventh day with symptoms of peritonitis (one vaginal examination five hours before operation).

Sepsis.—Primipara, aged twenty-nine years, in labor three days; cervix 3½ fingers dilated; membranes ruptured three days. Two-flap section performed. Uterus was full of meconium; endometrium green and necrotic. No temperature until third day postoperative, then bad chills, followed by temperature as high as 106° to 107°. Repeated blood cultures negative. Three blood transfusions given. Stitch-abscess, suppuration of wound and evisceration followed. Patient continued downhill in spite of therapy, and died sixteen days postoperative. In retrospect this patient's chances of survival would have been increased if she had been delivered by a Porro or Latzko cesarean section.

Psychosis.—Primipara, aged thirty-one years, admitted in sluggish labor with marked psychic disturbance. After thirty-eight hours of labor attended by uterine inertia, no dilatation or engagement was evident. Low cervical transverse cesarean section was performed. On second day postoperative although pelvic condition was satisfactory, patient became violent and had to be forcibly restrained. During the night patient got out of bed and became uncontrollable. Temperature 107°. Psychiatric consultation: toxic exhaustion psychosis. Patient died third day postoperative.

Perforated Peptic Ulcer.—Profuse painless vaginal bleeding six hours after onset of labor. Section performed and placenta found to completely cover the internal os. Moderate febrile convalescence for eleven days. On the twelfth day postoperative patient suddenly vomited large amount of dark red blood. Improved under sedative treatment. Several hours later she suddenly went into shock and died. Autopsy findings: Subacute duodenal ulcer with perforation and erosion of artery; massive gross hemorrhage into intestinal tract and stomach; puerperal gangrenous endometritis and abscess of the right broad ligament.

Pneumonia.—Patient, aged twenty-four years. Primipara with flat pelvis. In labor twenty hours; cervix two fingers dilated; floating head. Under spinal anesthesia, two-flap section done. Examination of chest revealed an extensive lobular pneumonia twenty-four hours later. Patient died on fourth day postoperative. No postmortem.

Pneumonia.—Primipara, aged thirty years, admitted in labor after having 3 convulsions at home. Labor pains for eight hours; one finger dilated; membranes intact. Patient complained of severe dizziness and blurred vision. Became irrational just after admission. Legs markedly edematous. Blood pressure 164/104. Albuminuria present. Classical cesarean section performed under general ether anesthesia. For four days postoperative her condition was fair, with normal temperature, blood pressure 150/80, edema disappearing, and fully rational. On the fifth day she developed signs of a right upper and middle lobe pneumonia. Her condition became worse, and finally coma ensued. Died on sixth day postoperative. No postmortem. In retrospect, it would appear that local anesthesia would have been preferable.

Pulmonary Infarct.—Patient, aged thirty-three years, para ii, gravida iii, admitted after twelve hours of active labor with membranes ruptured for thirty-six hours, and a prolapsed arm. Arm replaced. After twenty-four more hours of labor, the head did not engage. Low two-flap cesarean section performed. For the first three days after the operation, her condition was good. On the fourth day, she developed a pulmonary infarct, and died on the fifth day. No postmortem examination.

Pneumonia.—Patient, aged thirty-six years. Primipara with a history of rickets as a child, and a flat, rachitic pelvis, admitted for an elective cesarean section. Full term, not in labor; membranes intact. Classical section performed under ether anesthesia, which was taken poorly by the patient. On the day following operation, patient developed a temperature of 102.5°, pulse 150, respiration 34, with signs of pulmonary involvement (bronchopneumonia). Temperature kept mounting; course rapidly downhill, and died on fourth day postoperative of pulmonary edema following a fulminating bronchopneumonia.

Ablatio Placentae.—Patient, aged twenty-nine years, para ii, six and one-half months gravid, was admitted to hospital with severe abdominal pains accompanied by vaginal bleeding for four hours; moderate syncope. Abdominal examination revealed a uterus the size of a full-term pregnancy, markedly tense, ligneous in consistency. Fetal heart not heard. Cervix undilated and unprepared. Patient exhibited marked pallor; mucous membranes blanched; pulse rapid and thready. Diagnosis: ablatio placentae. Classical cesarean section. Transfusion on operating table. Patient did not react to intensive stimulation and died nine hours after the operation.

Nephritis Uremia.—Patient, aged thirty years, para iii, a deaf mute, admitted to hospital because of marked edema and dyspnea of one week's duration. Blood pressure 260/150, 3+ albuminuria. Not in labor. Membranes intact. Impression was that of a fulminating toxemia. After twenty-four hours of sedative and eliminative therapy, a classical cesarean section was performed. Living infant. Postoperative course smooth for two days. Pressure dropped to 175/110. On

third day after the operation, developed temperature of 103.4°, restless. Papilledema present. Total urinary output for twenty-four hours was seven ounces. Immediately thereafter she developed a complete urinary suppression and, despite all attempts to stimulate renal activity, died of uremia on sixth day after the operation.

COMMENTS

1. The number of incidental operations has been kept down to the minimum in our belief that it is good surgery not to do more than the cesarean section except in the presence of some urgent indication.

2. We are impressed with the importance of making the necessary decision to intervene in borderline cases before delayed operation with its morbid consequences, both maternal and fetal, nullifies the benefits of this type of delivery.

3. In repeat cases, we favor a moderate trial labor where the preceding operation has had an afebrile convalescence; and the primary indication has not been a bony dystocia precluding the possibility of subsequent vaginal delivery.

4. In our hands the low cervical two-flap operation has given the best results both as to lowest mortality and morbidity. The classic operation has been reserved for elective cases and low placental insertions not long in labor.

5. A recent valuable adjunct has been 0.5 c.c. of pituitary extract diluted with 4 c.c. of warm saline, instilled slowly into the vein in the elbow, as soon as the fetal head is delivered. This causes a prompt, firm contraction of the fundus uteri, with advantages threefold: conservation of the patient's blood, spontaneous separation of the placenta, and a clearer operative field. If given slowly in the above dilution, pituitary shock does not occur.

6. Past experience with unexpected abdominal delivery of a monster emphasizes the importance of a routine x-ray of the abdomen prior to operation.

I am indebted to all those members of the staff who have permitted me to utilize the records of their private patients as part of the survey. The major part of the preliminary data was assembled by Dr. Harry Ehrlich, and without his assistance this report would not have been possible. I wish to gratefully acknowledge the invaluable cooperation of Dr. Leo Schwartz, Chief of Staff, in the composition of this paper.

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875 ST. MARKS AVENUE

A REVIEW OF 226 CASES OF OBSTETRIC ANALGESIA*

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THE present survey of analgesia in obstetric patients is based on intensive study and personal observation during the past ten years. Only cases coming within recent experience, however, are reported in detail in this paper.

The series includes 226 cases drawn from private practice during the past two years (1934 to 1935 inclusive). They are unselected from every standpoint, except that they illustrate the effect of a pentobarbital-scopolamine-nitrous-oxide combination, in various dosages of each. The methods employed represent the outgrowth of experience with various successive types of analgesies, starting with the old twilight sleep formula, in 1925. As each in turn was abandoned, it was replaced by another which seemed to offer greater promise; and it is my earnest hope that a combination will be evolved which will even be superior to the one about to be described.

My purpose in presenting this report consists not only in outlining the general principles upon which the present plan of obstetric analgesia is based and the results obtained—but, more especially, in bringing out in more detail some personal impressions gained through close and constant supervision of the parturient woman.

The success or failure of amnesia in these cases is based upon the patient's own estimate; the classification in every instance being made on the basis of her judgment. Thus, cases were divided into one of three classes: either as "excellent," as "good," or as "failures." The designation "excellent" was applied when complete amnesia was attained in a patient who has no recollection of disagreeable pain. When the patient remembered severe pain, no matter for how short a time, the result was considered "good." A case was regarded as a "failure" when there was no amnesia for the greater part of the labor due to late administration or insufficient dosage.

A combination of pentobarbital-scopolamine and nitrous oxide was used in these cases. The end-results as judged by the patients' testimony were: "excellent" in 91 per cent of the entire series; "good" in 7 per cent; and "failure" in 2 per cent.

Of primary importance in any analgesia is the safety of mother and baby. No method which increases the obstetric hazard is to be tolerated. In this series there was no maternal death.

The infant mortality includes two cases (one for each of the two years), which gives a stillbirth rate of 0.9 per cent for the entire series. The first stillbirth was a case of cervical dystocia in a funnel pelvis,

*Read before the New York Obstetrical Society, May 12, 1935.

with a cord wound tightly around the neck, requiring a median forceps after a protracted labor. The second was a case of prolapsed cord. In neither of these cases could the result fairly be laid at the door of the analgesia.

The morbidity in this series, based on a temperature of 100.4° F. for any two days, not on the day of delivery, was 2 per cent. The morbidity based on 100° was 4 per cent. The morbidity was not serious in any of the cases.

The total number of forceps in this series is 57. This gives a forceps incidence of 25 per cent. These were distributed in the following manner: one high forceps, 16 median forceps, and 40 low or outlet forceps.

There were 3 cases of postpartum hemorrhage representing an incidence of 1.3 per cent; one of these patients was given a transfusion.

STUDY OF CASES FOR THE YEAR 1934

For the purpose of more detailed analysis, the year 1934 was studied as a unit. During that year there were 103 cases in which some part, or all, of the pentobarbital-scopolamine-nitrous oxide combination was used. There were 67 primiparas and 36 multiparas. The net result of the analgesia in this series was: "excellent" in 85.4 per cent; "good" in 10.8 per cent; and "failure" in 3.8 per cent.

There was no maternal mortality.

The infant mortality consisted of one case (previously described), a stillbirth rate of 0.9 per cent.

The morbidity in these cases, on the basis of 100.4° F., was 1.9 per cent. On the basis of 100° F. two additional cases must be added to the list, making a total of 4 cases, and a morbidity rate of 3.8 per cent.

The forceps incidence in this group was 35.9 per cent. Of the forceps deliveries 35 per cent were mid-forceps and 65 per cent were low forceps.

During labor, 56 of the 103 patients were examined vaginally, making a total of 74 examinations. Rectal examinations, which were not included in the figures just given, were usually made to determine the progress of the labor.

Episiotomy was done in 63 per cent of these cases.

The condition of the pelvic floor in the remaining 38 cases may be summarized as follows: 22 patients had no tear; 11 had a first-degree tear; and 5 had a second-degree tear.

The blood loss in these cases is of especial significance. The standard used for average bleeding is 200 to 300 c.c., less than average up to 200 c.c., and 300 to 500 c.c. more than average bleeding; beyond that it is described as postpartum hemorrhage. There was one postpartum hemorrhage, or 1 per cent; more than average bleeding occurred in 12.6 per cent; and in 71.8 per cent less than average bleeding occurred.

It is in most instances possible to dispense with inhalation ether during delivery when this method is used. This is an advantage in that it tends to eliminate one of the factors contributing to blood loss.

The influence of this method on the babies was calibrated by two factors: first, the amount of initial asphyxia, and the difficulty of resuscitation, and second, the progress of the infant as reflected by a gain or loss in weight. Breathing was delayed for more than the usual time in only six babies, and a mild form of resuscitation was used. Upon analysis of the weight charts, it was found that 71 per cent of the babies exceeded birth weight on the fourteenth day, and 29 per cent were below birth weight on the fourteenth day. The average gain was 175 gm. above birth weight, and the average loss, 130 gm. This type of analgesia has no effect on the immediate or remote course of the infant.

METHOD

The average first dose of scopolamine was $\frac{1}{150}$ gr., given in conjunction with an average first dose of pentobarbital of $4\frac{1}{2}$ gr. The average character of the pains when this first dosage was given consisted in contractions at an interval of four to five minutes, and having a duration of thirty to forty seconds. The average interval between the first and second dosages was $2\frac{3}{4}$ hours for primiparas and $1\frac{1}{4}$ hours for multiparas. The average second dose was $\frac{1}{200}$ gr. of scopolamine, and $4\frac{1}{2}$ gr. of pentobarbital. In prolonged labors, when a third dose was necessary, it averaged $\frac{1}{200}$ gr. of scopolamine and 3 gr. of pentobarbital.

The various dosages were distributed in the primiparas as follows: One dose was required in 34 per cent; two doses were given in 50 per cent; three doses were required in 15 per cent.

The multiparas required the following dosages: 80 per cent were given only one dose; 17 per cent were given two doses; and 3 per cent required three doses.

An effort was invariably made to individualize the patient, as far as the dosage was concerned. The dosage varied anywhere from one capsule ($1\frac{1}{2}$ gr.) of pentobarbital to six capsules (9 gr.) and $\frac{1}{250}$ to $\frac{1}{100}$ of a grain of scopolamine. All patients were tested before labor with pentobarbital to see if there was any idiosyncrasy to the drug but none was found.

ADVANTAGES AND DISADVANTAGES OF OBSTETRIC ANALGESIA

The foregoing results, I believe, compare favorably with the average similar private group in which analgesia has not been employed. However, these results do not convey any adequate idea of the difficulties encountered in their attainment. Published accounts of analgesia statistics with which I am familiar give the impression that the results are universally good if a certain set of drugs is administered in a more or less routine fashion. This has not been my experience. I have found it a very laborious and exacting task, and the more perfect the amnesia, the more laborious and exacting it becomes.

I would like to indicate some of the features which seem to me to be important in attaining a good result and I want especially to emphasize some of the potential disadvantages of the method.

At the outset, let us take the most burdensome feature, namely, the necessity for the constant presence of the obstetrician. This is of course a primary disadvantage, but it is my conviction that it is very essential to successful analgesia. So numerous are the factors requiring his personal interpretation, that his presence is imperative. I have been consistently unsuccessful in the "remote control" of analgesia.

To illustrate how this is linked up with the process I will point out one important feature in this work, namely, the psychic attitude of the patient. An agreeable, relaxed, fearless mental state as opposed to a tense, fearful one is desirable before the first dose is given. This can be best attained through the reassuring presence of her physician. She is not so likely to fight the sedative, there is less fear, and the drug is more successful in its effect.

Another important feature is the postponement of the first dose. To neutralize perhaps the greatest handicap of this form of analgesia, namely the slowing of labor by the depression of the force of and the lengthening of the interval between the uterine contractions, one must be particularly cautious with the first dose. It has been reported that pentobarbital accelerates the first stage of labor. It has been my experience that pentobarbital or any sedative, given too early in labor, will lengthen the period between contractions and prolong the labor. For this reason it is desirable to delay the administration of the first dose, especially in primiparas, to an optimum point of rhythm and intensity of the pains, but not to a point of severe discomfort. Each patient offers an individual problem in her reaction to pain; but all have this common denominator, that if they know complete relief is available and theirs for the asking, and that their consciousness of these pains has a limit which is more or less in their hands, they are content to endure them for a longer time, without complaint, than they otherwise would. In this way the doctor is not stampeded into giving an early initial dose.

The problem of initial dosage in the average case is not so much a question of amount, as a question of time. In the primipara with plenty of time ahead of her, and with slowly developing pains, the first dose should effect some sedation but, more important, it should lay the groundwork for the doses to follow. In the multipara, who is more expeditious in her work, the object of the first dose is to effect amnesia, if possible, before the development of strong pains. The amount of the first dose is therefore usually larger for the multipara than the primipara and is also given earlier.

An examination of the patient at this juncture is in order. Information on two important points is essential, namely, what the patient is doing at the moment; and second, what you may expect her to do in the immediate future. The former concerns the initial dose; the

latter has to do with subsequent doses, and their relationship to the first. By examination, I refer to vaginal examination.

Since time is the important feature in analgesia, by the same token, the evaluation of the resistance to the advancing part and the amount of energy being developed to overcome this resistance are equally important. The cervix and the contraction tell the greater part of the story. When the cervix is long and thick, it is best to postpone the first dose until there is some retraction and dilatation.

Individual pain reaction to the same mechanical force is a variable entity. Both the contraction and the complaint must be taken into consideration. But if the contraction is feeble and the complaint great, a smaller dose is advisable.

In spite of careful supervision, delayed labor due to analgesia may occur. Then it becomes necessary to stimulate labor, maintaining the narcosis. Nothing is more discouraging for a patient than to wake up and to realize that the worst is ahead, rather than behind her. If a mistake has been made and the labor definitely slowed, there are three ways in which it can be stimulated: (1) by small doses of pituitrin (usually two minims); (2) by rupture of the membrane; and (3) by flexing the extended head. All of these methods are not without hazard. If the first dose is given at the right time, these procedures will not be necessary. The following procedure is of great value in expediting labor when it has been delayed by too early or too much analgesia: The patient is placed in the extreme lithotomy position, the head is flexed to as great a degree as possible, and at the same time an attempt is made to push it downward and backward toward the hollow of the sacrum. This in many instances corrects the direction of the force and, in so doing, renders the contraction more efficient, and may considerably reduce the time of labor. Induced labors offer the highest potential for delay by analgesia. In cases where pelvic dystocia is expected, one should be cautious in administering the first dose.

Once the analgesia has been established, it should be maintained until after delivery. It is the maintenance of this state that calls for successive doses. It is sometimes difficult to tell whether or not the patient is conscious. Incoherence of speech or thought, even though occasionally interspersed with rational conversation, usually indicates that there will be no subsequent memory of the labor. When it is suspected that the analgesia is not complete, it is occasionally advisable to anesthetize the patient with nitrous oxide. This should be given continuously, over a period of from five to ten minutes. Outside stimuli are cut off from the patient by this means, the effect of the sedative is reinforced, and prolonged analgesia results. Advantage may be taken of this nitrous oxide administration for an examination.

Restlessness is one of the great disadvantages of this method of analgesia. Pentobarbital may be increased without the scopolamine, which tends to quiet the patient. Occasionally, in cases of extreme restlessness, rectal ether may be used with good results. Competent nursing supervision is always essential, both before and after delivery, until the patient is completely awake. This, of course, complicates the nursing problem, but it is a virtue in another direction, in that it insures continuous care of the patient.

In this entire series there has been but one injury. One patient bruised her lip. That was the extent of the self-inflicted trauma.

The time of delivery is the point at which restlessness becomes a personal problem for the obstetrician. There is a tendency to control this with complete narcosis and to terminate labor with forceps. This is unnecessary, as the patient can be restrained on the table, with the use of a small amount of nitrous oxide. There is no diminution in the natural expulsive forces during the second stage.

In order to determine the validity of this belief, an effort was made, in 1935, to allow as many cases as possible to terminate spontaneously. The necessity of employing forceps dropped from 35.9 per cent in 1934 to 16 per cent in 1935. The use of low forceps in these cases is a concession to the peace of mind of the operator, and not a necessity for the patient.

An increase in the tendency toward asphyxia of the baby is popularly ascribed to this procedure. It should be emphasized that nothing of this nature was observed in any case in the series. In fact, no deleterious effects were noted in cases in which the terminal dose was given just before delivery. The babies flourish and gain in the post-partum period, and the likelihood of their having brothers and sisters at an early period is an attribute of analgesia which should not be disregarded.

This series will illustrate the obstetric results that may be obtained coincidentally with successful analgesia. Obstetricians seem to be divided into two classes: those who do not use analgesia, and those who use it and write about it. The former are extravagant in their criticism; the latter, in their praise. The former believe that analgesia retards and complicates labor, the latter insist that the reverse is true. I would like to place myself somewhere between the two groups. The fact should be emphasized that, above all, this method calls for individualization of the patient, each one being regarded as a distinct clinical unit. It will be noted that no attempt has been made to standardize either the dosage or the time intervals, for the reason that no general rules are possible in this connection. The successful administration of these drugs requires the constant presence and taxes the skill of the most experienced in this field. The ultimate object is the creation of complete amnesia without affecting the course of labor.

This is in most instances no simple feat. While probably no one will doubt the possibility of attaining complete amnesia, its accomplishment, unattended by disagreeable features, is a goal which one can hope to attain only as a result of infinite patience combined with considerable experience.

To summarize briefly the important conclusions:

1. Perfection in analgesia has not been attained.
2. Individualization of each patient is essential.
3. Constant medical and nursing supervision is imperative.
4. Each patient should be tested for idiosyncrasy to the drug before labor.
5. Restlessness can be a disagreeable feature of this analgesia.
6. Blood loss is not increased by this method of analgesia.
7. The length of labor need not be increased by this analgesia.
8. Forceps incidence need not be increased.
9. Mental trauma is definitely decreased.
10. In the hands of a competent obstetrician it is a safe analgesia for mother and baby.

1088 PARK AVENUE

DISCUSSION

DR. GEORGE H. RYDER.—Amnesia in labor has been attained by Dr. Damon in 91 per cent of his cases. This is a high percentage, and it has been attained with no maternal loss and with a very low fetal mortality. In a larger series it is conceivable that such nearly perfect results might not hold. His incidence of forceps operations, 25 per cent, is not high for private patients, more especially when 70 per cent of the forceps were of the low variety. His incidence of postpartum hemorrhage, 1.3 per cent, is also not unduly high.

I do not believe, however, that amnesia in labor is the goal for which obstetricians are striving. Rather is it *painless* labor. This is not the loss of memory of pain, but rather no pain to remember. These patients with amnesia probably suffer as much as or more than those delivered in other ways. It is simply that they forget the pain they have had. I wonder what effect pain has on the nervous systems of patients temporarily deranged mentally. Possibly none. But we do not know.

There are serious disadvantages to amnesia during labor. Dr. Damon mentions the extreme restlessness and excitability, calling for constant surveillance and restraint. In one unguarded moment on the part of an attendant, the patient may jump out of the window or do herself other bodily harm.

Already we have at hand many measures for easing the pain, none ideal, but many nevertheless very helpful. Morphine is a drug too little used. It has been demonstrated recently that morphine does not diminish uterine contractions and therefore it should be a most useful drug in labor, for it certainly does lessen pain. Morphine, $\frac{1}{4}$ gr., early when the pain is becoming troublesome, is most helpful, and in long labors it may be repeated safely. It does not harm the fetus unless given just before birth when it may depress the respiratory center.

Analgesia in labor has come to stay. It is a product of civilization. Wisely used, it does not increase maternal mortality, nor fetal mortality. Nor does it add to birth injuries or fetal damage, or cause an increase in operative interference.

DR. ALBERT H. ALDRIDGE.—On the service at the Woman's Hospital, we are using routinely the same combination of drugs and in practically the same dosage which Dr. Damon has employed in the series which he has just reported.

I agree with Dr. Damon that success and safety in the utilization of analgesic drugs during labor depend upon testing a patient before the onset of labor to detect a possible idiosyncrasy to the drugs to be used; on gaining the confidence of the patient during the antepartum period and early hours of labor; on avoidance of any medication until labor is well established; on the selection of proper dosage of drugs to fit the type of labor and on the careful study of the patient's reaction throughout labor. If these precautions are observed analgesic drugs in adequate dosage may be used routinely during labor with safety to the mother and baby, and without disturbing the normal processes of labor.

Dr. Ryder has referred to possible undesirable after-effects on the personality of patients who have been temporarily deranged by use of drugs which cause amnesia and analgesia. It is our impression, however, that the satisfactory postpartum condition and rapid convalescence of patients who have been spared fatigue and mental trauma of labor is the most convincing evidence against such criticism and of the value of such drugs to the mother.

DR. JOHN E. TRITSCH.—I agree that when we speak of obstetric analgesia we are usually referring to obstetric amnesia. When we arrive at the perfect analgesia, we will have arrived at something that actually eliminates pain, not merely the recollection of pain. To accomplish this we shall have to devise some means by which the sensory fibers coming from the uterus will be paralyzed, whereas the sympathetic fibers which produce contraction, as well as the local contraction initiating centers in the uterus, will be uninfluenced by the treatment. We have used the barbiturates with scopolamine at the Fifth Avenue and Metropolitan Hospitals many times and have failed to produce analgesia, so that, as a consequence, we are now more inclined toward the use of rectal ether with the barbiturates. We have been using the acid form of the barbiturates, as, for example, amytal, pentobarbital and allurate in the acid form, which dissolve in ether, with which we think we get a little more uniform absorption of the substances. We feel also that we control the excitation which has been referred to, to such a degree, that we practically never have any patients who are excited sufficiently to cause trouble. However, we still have occasionally a patient who is partially anesthetized and consequently must be constantly watched.

I noted that in Dr. Damon's experience, the duration of the action of the drug in primiparas was two and three-fourth hours and in multiparas one and one-fourth hours, which required repetition of treatment in many cases. With the barbiturates in ether the necessity for repetition is very rare. In almost all of our cases we get six to eight hours of analgesia and the necessity for repetition has occurred only two or three times in a series of several hundred cases.

In primiparas the longer acting barbiturates will probably be more desirable and the shorter acting ones in the multiparas. We have recently been experimenting with evipal rectally, in combination with rectal ether, and found that we got about three or four hours of analgesia. We got six or eight hours with the longer acting barbiturates. Pentobarbital falls in a class between evipal and the longer acting drugs, such as amytal and allurate. When we used evipal in primiparas, the patient frequently came out of the analgesia long before the time of delivery, whereas, when we used it in multiparas, the action was sufficiently long to accomplish the desired result. So we feel that investigation, as far as parity and expectancy of time of delivery, is an important element.

We also feel that the multiparas have to a certain extent been neglected in connection with our attempts at alleviating labor pains, primarily because of the fact that they frequently have precipitous labors. To patients who come to the hospital just about ready to deliver we just give nitrous oxide. The use of nitrous oxide in the second stage of labor is a prerequisite to the satisfactory relief of pains of labor, while the analgesics and amnesics are primarily for use in the first stage.

FURTHER OBSERVATIONS WITH DIAL URETHANE FOR OBSTETRIC ANALGESIA

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IN OCTOBER, 1934, a preliminary report was made on the use of dial urethane solution for obstetric analgesia.² The results up to that time had been very satisfactory, but the limited number of cases in which the preparation had been used rendered caution necessary in drawing conclusions. In the two years that have elapsed since the submission of this report, the opportunity has occurred to employ the solution in 198 cases more, so that the series now numbers 254. The additional experience gained during this time has served to strengthen certain of the earlier impressions gained, but has led me to modify some of the views expressed in the preliminary paper. Because of these facts, it was felt that a supplementary report might possess sufficient interest to justify its publication.

As previously explained, the dial urethane solution contains 10 per cent dial (diallyl-barbituric acid) and 40 per cent urethane, and is available in 2 c.c. ampules. Obviously, to refer to it merely as "dial" is incorrect, because the urethane present must contribute something, at least, to the action. Intravenous administration has been employed in all the cases forming the basis for this report. That this method of administration is essential for truly effective analgesia, I am convinced by my own experience with intramuscular injection, and also by the indifferent success following intramuscular injection as reported by McNeile and Vruwink⁹ and by Rund.¹³ It is true that a certain element of danger is always present when intravenous injection is practiced, but that this danger is sufficiently great to render unwise the careful and intelligent intravenous injection of the dial urethane solution has certainly not been indicated by my experience nor, apparently, by that of any other authors who have employed it in obstetric patients. I cannot, however, too strongly emphasize the necessity of scrupulous care in carrying out the injection; it is not a procedure that may be safely delegated to nurse or inexperienced interne, but should be made by the obstetrician himself or under his direct supervision.

The question of correct dosage is, of course, of great importance. The first consideration is the safety of the patient, but, while keeping this always in mind, one should avoid the mistake of so limiting the dose that satisfactory analgesia consistently fails to develop. In my first cases, the dosage recommended by Nelson¹¹ was employed. Satisfactory results were obtained in a certain proportion of the cases, but failure so often occurred that I soon became convinced that larger amounts of the solu-

tion were frequently necessary. Birnberg and Livingston,¹ likewise, found Nelson's dosage insufficient, stating that "all patients required at least 4 c.c. before any appreciable effect was seen"; because of which they arbitrarily adopted 4 c.c. as initial dose, regardless of weight or other individual peculiarities. As regards subsequent administration of the solution, these authors attempted some individualization, considering no further injections necessary if delivery occurred within an hour after the first dose and omitting the third injection "if the patient was markedly narcotized after two doses." Weight, too, according to them, should be given due consideration: patients of 125 pounds or less receiving only 2 c.c. in second or third injections, while those weighing 170 pounds or more received routinely 4 c.c.

The maximum narcotic effect of dial develops almost immediately after entrance of the drug into the blood stream. Taking advantage of this fact, Garcia³ employed what was subsequently designated by Holtermann⁴ as "biological dosage," injecting the solution intravenously at a slow rate until the patient lapsed into unconsciousness. Although unfamiliar at that time with the work of Garcia and Holtermann, it soon became evident to me that individualization in dosage was not only desirable but actually necessary if satisfactory analgesia was to be secured and, at the same time, the safety of the patient taken into consideration. Weight, alone, is not a safe guide in determining dosage. As a general rule, the heavier the patient, the larger the effective (and safe) dose of dial urethane: this is far from being invariably the case; indeed, I have found that not infrequently the larger patients are of a more phlegmatic type and respond more readily to the action of the preparation than is sometimes the case with smaller, highly nervous individuals. A technic was soon developed, which is still adhered to so closely that the description given in my earlier report may be quoted in full:

The patient is told that she will feel relaxed and sleepy from the injection; a matter of some importance, because, otherwise, alarm may be experienced over the peculiar sensation. Four cubic centimeters of the solution are drawn up into a 5 c.c. syringe and the needle thrust through the vein wall. Injection is made slowly, the patient being constantly questioned and the injection discontinued when she no longer responds. In some cases, 2 c.c. of the solution will suffice; in others, it may be necessary to inject the full 4 c.c.; I have never given in excess of this latter amount in any single injection. If sound sleep does not occur between pains, a second injection of 2 c.c. is given in thirty minutes. Further injections, each of 2 c.c., may be given, but I have not exceeded a total of 8 c.c. in the course of any labor.²

With added experience, I have become convinced that it is sometimes desirable and also safe to increase the dose above the limits set in the preliminary report, both for initial and total injections. This conclusion has not been arrived at hastily; it has been rendered possible by considering various published reports on the dosage of the solution and also by carefully feeling my way, slightly increasing the volume injected in

"refractory" patients, with constant careful observation of the immediate and possible delayed reaction in such cases. Again let me emphasize the need for scrupulous care in selection of dose and in attention to technic of administration: it must always be borne in mind that active drugs are being introduced directly into the circulation and one should not forget the disastrous results that followed the reckless advocacy of enormous doses of another barbiturate intravenously for the induction of surgical anesthesia. My earlier limitation of 8 c.c. for total dosage was set because of the reported experience of Nelson,¹¹ Hoven,⁵ and Muller.¹⁰ The first mentioned of these authors found that it was seldom necessary to equal this dosage in obstetric patients; and Hoven and Muller, from their observations on the use of dial urethane for "nareo-sustained therapy" in insane patients, considered it unwise ever to exceed a total dosage of 8 c.c. during the course of twenty-four hours. However, not only I found Nelson's dosage often inadequate, but Birnberg and Livingston,¹ as previously mentioned, came to a similar conclusion. Regarding Hoven and Muller's papers, it should be borne in mind that conditions present in cases under nareo-sustained therapy are vastly different from those to which the parturient woman is subjected: in the former, a state of partial or complete narcosis exists for several days; moreover, these insane patients are given fairly large doses of scopolamine along with the dial urethane. In rare instances it may be advisable to inject more than 4 c.c. for the initial dose in obstetric patients; however, this should be done only when the individual has failed to respond to the former maximum of 4 c.c. *when injected at a rate not to exceed 1 c.c. per minute.* Observing the precautions that have been stressed, I have never encountered an instance of either respiratory or circulatory depression in the sense generally used, nor have I seen any cases where late results attributable to the unfavorable influence of the medication were present. Birnberg and Livingston,¹ also, observed no deleterious effects after initial doses of 6 c.c. and total doses of 12 c.c. although it is my belief that their fixed-dosage method is less dependable and not as safe as the elastic one employed in my series.

The criteria for judging the effectiveness of the dial urethane solution have been analgesia and amnesia. Analgesia is graded as good, fair, or poor: amnesia as complete, incomplete, fair, or absent. The only disadvantage, from the maternal standpoint, so far encountered has been restlessness, either mild or amounting to actual mania: while, as regards the infant, the only undesirable effect of the medication clearly established is that occasionally involving the respiration.

Of the 254 patients, one was given a total of only 3 c.c. of the dial urethane solution, with good anesthesia and complete amnesia; however, the patient was para iii and labor lasted only three hours. Seven patients were given a total of 4 c.c., with good analgesia and complete amnesia in six instances, and fair in the seventh. A total dosage of 6 c.c. was employed in 22 patients, with good analgesia in 20, fair in 1, restlessness in 1, complete amnesia in 19, and fair in 3. With a

total dosage of 8 c.c. in 79 patients, good analgesia was obtained in 63; fair analgesia in 13, poor analgesia in 1, complete amnesia in 77, fair amnesia in 1, no amnesia in 1, mild restlessness in 1, and mania in 1, this being the only case in the series that was maniacal and required physical restraint. Eighteen patients were given a total dosage of 9 c.c. with good analgesia in 17 and fair in 1; amnesia was complete in all, and there was no instance of restlessness recorded. The total dosage of 10 c.c. was given to 95 patients, analgesia was good in 83, fair in 6, and poor in 1, while amnesia was complete in 92 and fair in 3. Restlessness was noted in 5 patients after this dosage. After a total dosage of 12 c.c. in 31 patients, analgesia was good in 24, fair in 3, and poor in 1, while amnesia was complete in all and restlessness was noted in 3 cases. One patient, a primipara, was given a total of 14 c.c. during the course of a thirty-six-hour labor, with good analgesia and complete amnesia. Engagement not having occurred at the expiration of this time, section was performed and a posterior fibroid, large enough to prevent entrance of the head into the pelvis, was found. Although the patient took food and water during labor, she had no recollection of events occurring during labor, including her transfer to the operating room and administration of inhalation anesthesia.

Analysis of my data reveals the interesting fact that results were independent of the size of the dose of dial urethane employed. Thus, after a total dosage of 4 c.c., good results were obtained in 85.7 per cent of the cases; after 6 c.c., in 90.9 per cent; after 8 c.c., in 78.4 per cent; after 9 c.c., in 94.4 per cent; after 10 c.c., in 87.3 per cent; and after 12 c.c. in 77.4 per cent.

This serves to stress the fact that elasticity in dosage, allowing individualization, is most important, because by means of its intelligent application one is able to avoid the danger of needlessly administering large amounts of the analgesic and, at the same time, is reasonably sure of obtaining effective analgesia and amnesia. My experience establishes, I believe, that it is unwise to adopt any fixed rule for dosage that should apply to every individual, regardless of constitutional differences: the dose should be adapted to the individual, but should rarely exceed 4 c.c. at the first injection or 12 c.c. as total amount during the labor. I should certainly feel considerable hesitation about giving an initial injection of as much as 6 c.c.; fortunately, none of my patients has been so refractory as to require more than 5 c.c.; indeed, as already mentioned, in practically all cases, 4 c.c. or less will suffice as initial dose.

Obviously, physicians and patients both will vary in their estimation of the efficacy of an analgesic. When a patient rests quietly between pains and merely moves slightly and moans while the uterus is contracting, I have considered analgesia as "good," but only "fair" if she is conscious and talkative in the interval during pains. Restlessness deserves especial consideration; I have classed it as "mild" if the patient moves constantly or intermittently in the absence of pains. However, it should be borne in mind that the patient under the influence of an effectively analgesic dose of dial urethane should never be left alone for a moment, but should constantly be under the supervision of a responsible attendant, preferably a physician or trained nurse. These patients are, at best, semiconscious, and one never knows when they may roll out of bed, or, indeed, develop mania, although this latter

occurred in only one of my series. In my earlier report,² approving reference was made to the condemnation by Irving, Berman, and Nelson³ of opium derivatives as obstetric analgesics, but in the short time that has elapsed since then, I have come to modify my views on this point to a certain degree. While still feeling that opium derivatives are absolutely contraindicated in the multiparous patient and also in the later stages of labor in primiparas, I now am of the opinion that in the exceptional, nervous, apprehensive primipara, just the one who is likely to respond least favorably to dial urethane medication, the *early* administration of a third or even two-thirds of a grain of pantopon exercises a most beneficial effect and, apparently, is most serviceable in preventing the later occurrence of restlessness. This is in harmony with the observation of Birnberg and Livingston¹ that very small doses of morphine (gr. 1/20 to gr. 1/12) prevented excitement and restlessness in their patients who had received dial urethane.

As to respiratory depression of the infants from the action of the dial urethane solution, this is rarely of a severe nature. In the 254 deliveries, there were three pairs of twins, making a total of 257 infants, two of whom were stillborn, but both had apparently died some time before onset of labor, maceration being present. In the remaining 255 infants, spontaneous respiration occurred without delay in 220; 25 infants showed mild depression of respiration; and 10 required rather active measures for resuscitation. As brought out in the recent excellent paper by McGrath and Kuder,⁵ haste and overzealous therapy should be avoided in these infants. Care should be directed toward removal of mucus, amniotic fluid, or other foreign material from the air passages, either through postural drainage or, when necessary, by actual suction. The character of the heart action is a far better guide as to the gravity of the condition than the color of the skin or the length of time before respiration starts. It should be borne in mind that artificial respiration, when necessary, must be performed with care; "even mouth to mouth breathing may inflict serious injury." My experience with coramine as a respiratory stimulant in the severer cases of depression has been particularly happy. When clearing out the air passages, mild cutaneous stimulation and careful artificial respiration have not been successful in establishing natural breathing; $\frac{1}{2}$ c.c. of coramine injected into the umbilical vein has, invariably, proved effective. The possibility of overexcitation of the central nervous system by this dosage, suggested by McGrath and Kuder,⁵ has not been established by my experience, and instead of manifesting the depressing action of lobeline on the circulation, pointed out by Moncrieff and others, coramine acts as a circulatory "stimulant," as indicated by the improvement in the character of cardiac action and in the color of the skin almost immediately after intravenous injection. Both the safety and the efficacy of coramine when used for respiratory stimulation are estab-

lished, not only by my rather limited observation but by the much more numerous clinical data presented in the papers of Wood,¹⁴ Reese,¹² and Lundy⁷ in this country and by a large number of foreign authors. However, I subscribe fully to the statement by McGrath and Kuder⁸ that "no drug therapy provides the fundamental clearance and patency of the air passages."

Few additional comments are necessary. Added experience has strengthened the belief that dial urethane analgesia generally hastens cervical relaxation and shortens labor, although rare instances are encountered where the reverse seems true. I have had no reason to alter the earlier expressed opinion that this form of analgesia is *not* contraindicated in the presence of respiratory tract infection; I have employed the preparation in ten such cases with very satisfactory results and no apparent deleterious effects. Delayed recovery of consciousness has not been an inconvenience in my series; even during labor, it is generally possible to rouse the patients sufficiently to have them take liquids.

Dial urethane is not the ideal obstetric analgesic; its safe and successful employment demands an exacting technic and constant supervision of the patients; preferably, within a hospital. Success does not invariably result even when these conditions are complied with, but it has certainly proved the most generally satisfactory agent with which I have had experience. Respiratory depression of the mother has not been encountered, and in the comparatively few instances where this occurred in the infants, clearing out the air passages, mild cutaneous stimulation, carefully performed artificial respiration, and intravenous injection of 0.5 c.c. of coramine, alone or combined, have been successful in every instance.

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TUMORS OF THE OVARY

A STUDY OF 1,101 CASES OF OPERATIONS FOR OVARIAN TUMOR

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THIS paper presents an analysis of laboratory and clinical data from 1,101 cases of ovarian tumor operations performed at the Mount Sinai Hospital during the period from 1924 to 1935. The facts, derived from tables too extended for publication, are at variance with textbook concepts in many instances. These are of interest to the clinician and surgeon.

The tumor types are differentiated by pathologic classification; records without microscopic reports have not been incorporated in this study. Small groups of endometriosis of the ovary and tuboovarian cysts have been included, since the ovary was completely involved.

The frequency of benign tumors as well as carcinomas and sarcomas is given. Age groups by decades are presented in order of tumor incidence and tumors of the first, second, and third frequency are noted. Conversely, tumors are considered from the standpoint of incidence in all decades.

Uterine bleeding, dysmenorrhea, and menopause are studied in relation to the various tumors.

Metastases found at operation indicate the belated onset of symptoms and the foci are grouped by location in body systems. Complications of malignancies are discussed.

Symptoms, grouped under body systems, indicate that almost any abdominal condition may be simulated. The relation between the site of the pain and the site of the ovarian tumor has also been determined. Sedimentation rates are considered briefly.

Neither syphilis nor actinomycosis are found in this series.

The need for a single complete, organized statistical study is indicated by the absence of such a report from the literature.

I. INCIDENCE OF EACH TYPE OF OVARIAN TUMOR (TABLE I)

A. *Common Types.*—*Simple Cysts:* The 522 cases of simple cysts constitute 47 per cent of all ovarian tumors (1,101). These are the most frequent tumors of the ovary and are made up of follicular (76 per cent) and corpus luteum (24 per cent) cysts.

The follicular cysts are pathologically reported as hydrops, cystoma, follicle cysts, microcystic ovary, simple cystadenoma, and fibroepithelial cysts.

Eight per cent of all simple cysts contain intracystic hemorrhage, 80 per cent of these cases are found in corpora lutea cysts.

Intracystic hemorrhage takes place in 29 per cent of corpora lutea and in only 3 per cent of follicle cysts.

Dermoid Cysts: Although second in order of frequency, this tumor shows an incidence of 31 per cent less than the simple cysts. There are 182 tumors representing an incidence of 16 per cent.

Two of these tumors (1 per cent) revealed malignant change arising from the squamous cell epithelial structures within.

Papillary Serous Cystadenocarcinoma and Cystadenoma: It is significant that this ovarian cancer occupies a position of such high incidence. It is third in order of frequency and comprises 152 instances or 14 per cent of all ovarian neoplasms.

The benign form of this growth occurs four times less frequently; namely, 36 instances among all tumors, or an incidence of 3 per cent. This suggests the insidious nature of these growths and in most cases that recognition occurs after malignant change has set in.

TABLE I. INCIDENCE OF OVARIAN TUMOR TYPES IN 1,101 CASES

A. Common types:		1,063	
Simple cysts	522		47%
396 follicular			
126 corpus luteum			
Dermoid cysts	182		16%
Papillary serous cystadenocarcinoma	152		14%
Papillary pseudomucinous cystadenoma	64		6%
Endometriosis of the ovary	43		4%
Papillary serous cystadenoma	36		3%
Tuboovarian cyst	29		2.6%
Fibroma	24		2%
Papillary pseudomucinous cystadenocarcinoma	11		1%
B. Rare carcinomas		19	1.7%
Colloid or Krukenberg tumors	6		
Medullary carcinoma	6		
Carcinosarcoma	1		
Solid carcinoma	3		
Squamous cell carcinoma in a dermoid cyst	2		
Undetermined carcinoma	1		
C. Sarcomas:		9	0.8%
Spindle cell sarcoma	1		
Fibrosarcoma	4		
Round cell sarcoma	1		
Hemangiosarcoma	2		
Angiosarcoma	1		
D. Embryonal tumors:		10	1.0%
Teratoma	8		
Disgerminoma	2		
Total		1,101	

Papillary Pseudomucinous Cystadenoma and Cystadenocarcinoma: These tumors are infrequent. The benign form was found in 64 patients, an incidence of 6 per cent, and the malignant form occurred 6 times less frequently, namely, in 11 patients, or an incidence of 1 per cent.

Early reports on the benign pseudomucinous tumors reveal a high incidence. The wide variance between old and recent reports may be due to present routine microscopic examination of tumors.

Serous ovarian tumors are $2\frac{1}{2}$ times more frequent than the pseudomucinous growths. The papillary serous cancers are 14 times more frequent than pseudomucinous cancers but the benign serous growth is found only half as frequently as the benign pseudomucinous tumors.

Endometriosis of the Ovary and Tuboovarian Cysts: Forty-three instances of endometriosis represent 4 per cent of all ovarian tumors.

Tuboovarian cysts, 29 in number, constitute 3 per cent of all ovarian tumors.

These small groups are included because the ovary was sufficiently involved to warrant surgical removal.

Fibroma of the Ovary: This growth was found in 2 per cent of all ovarian tumors; 24 patients were operated upon.

B. Rare Carcinomas: nineteen tumors constitute 1.7 per cent of all ovarian growths. These are made up of 6 colloid or Krukenberg tumors and 6 medullary growths, 3 solid carcinomas, 2 squamous cell carcinomas arising within dermoid cysts, 1 carcinosarcoma and an undetermined malignancy.

C. Sarcomas: Less than 1 per cent of all ovarian tumors are sarcomas. In this series, only 9 were found; 4 fibrosarcomas, 2 hemangiosarcomas, and 1 each of spindle cell, round cell, and angiosarcoma.

D. Embryonal Tumors: In this group are 10 tumors, constituting 1 per cent of all ovarian growths. There are 8 teratomas and 2 dysgerminomas. Several of the former were recorded as teratoblastomas.

II. THE INCIDENCE OF OVARIAN MALIGNANCY (TABLE II)

There was 17.3 per cent malignancy among 1,101 ovarian tumors; 16.3 per cent were carcinoma and 1 per cent were sarcoma, representing 191 cases in all.

TABLE II. INCIDENCE OF MALIGNANCY OF THE OVARY
(IN ORDER OF FREQUENCY)

TYPE OF MALIGNANT GROWTH	NO. OF CASES	PER CENT OF MALIGNANCIES
Papillary serous cystadenocarcinoma	152	80.0
Papillary pseudomucinous cystadenocarcinoma	11	5.8
Colloid (Krukenberg) carcinoma	6	3.0
Medullary carcinoma	6	3.0
Fibrosarcoma	4	2.0
Solid carcinoma	3	1.6
Squamous cell carcinoma in a dermoid cyst	2	1.0
Hemangiosarcoma	2	1.0
Other rare sarcomas	5	2.5
Spindle cell sarcoma		
Round cell sarcoma		
Carcinosarcoma		
Angiosarcoma		
Total number of malignancies in 1,101 ovarian tumors	191	or 17.3%
Carcinomas	180—16.3%	
Sarcomas	11— 1.0%	

One hundred and fifty-two papillary serous cystadenocarcinomas represent 80 per cent of all malignant ovarian tumors. This growth is third among all ovarian growths and is 14 times more frequent than the pseudomucinous carcinoma, which was found only 11 times, an incidence of 5.8 per cent. The benign form of the latter is 6 times more frequent.

Both medullary and colloid cancers total 6 instances each, or 3.2 per cent of all ovarian malignancies. Various types of sarcomas range from $\frac{1}{2}$ to 2 per cent incidence among malignancies; the fibrosarcoma, 4 in number, is most frequent.

Cancer and Sarcoma Incidence Among Malignancies: 95 per cent of malignancies are carcinoma, and 5 per cent sarcoma. There were 181 and 10 cases, respectively.

III. AGE INCIDENCE AMONG OVARIAN TUMORS

Simple Cysts.—(522 cases.) Most of these tumors were found in patients between thirty and forty years of age. There were 189 patients representing 36 per cent of all simple cysts. There were 162 patients, or 31 per cent, in the twenty- to thirty-year age group, and 81 patients or 15 per cent were between forty and fifty years. Thus, 82 per cent of simple cysts occur between the ages of twenty and fifty years.

In young women between ten and twenty years of age, there were 77 instances, or 14 per cent incidence of simple cysts, among which corpora lutea, principally, constituted the pathologic findings. Sixty-five of these patients, namely 90 per cent, were young women of early menstrual age between ten and sixteen years.

Forty-four per cent of all simple cysts were found in patients under thirty years of age. The oldest patient in the group was sixty-nine years of age and the youngest twelve years of age.

Dermoid Cysts.—(182 cases.) The largest number, namely forty per cent of these tumors, is found in the third decade. Next in frequency is the thirty to forty-year age group, in which 55 patients, or 30 per cent of all dermoid cysts were found. The fifth decade shows 24 instances, or 13 per cent incidence. Thus, 83 per cent of dermoids are found in a combined age group between twenty and fifty years. The youngest patient was two years old; the oldest was seventy years of age.

Papillary Serous Cystadenocarcinoma.—(152 cases.) This tumor is found principally in women between the ages of forty and fifty years. Thirty-six per cent, or 55 patients, were operated upon. The sixth decade, fifty to sixty years, shows forty such tumors, or 26 per cent incidence, and the thirty- to forty-year age group shows a 22 per cent incidence or 34 cases. Thus, 84 per cent of these tumors occur in patients between the ages of thirty and sixty years. It is the most frequent type of malignancy of the ovary. This growth predominates over all other tumors in the seventh decade: 6.5 per cent or 10 tumors are found. A patient twenty-four years of age was found to have this ovarian cancer; the oldest patient was seventy years of age.

Papillary Pseudomucinous Cystadenoma.—(64 cases.) In this small group, 30 per cent or 19 instances were found in patients between thirty and forty years of age; fifteen per cent or 23 patients in the third decade and 20 per cent or 13 patients in the forty- to fifty-year decade. Thus 65 per cent of these tumors occur in women between the ages of twenty and fifty years. In young women between the ages of ten and twenty years, there were 7 cases or 12.5 per cent. The oldest patient in whom this tumor was found was sixty-eight years of age, the youngest was fourteen years.

Endometriosis of the Ovary.—(43 cases.) The greater number, namely 72 per cent, of these growths are found in the two decades between twenty and forty years; however, in the combined periods between twenty and fifty years, 93 per cent of all these tumors are found.

Papillary Serous Cystadenomas.—(36 cases.) Sixty per cent or 22 instances in this small group of benign neoplasms are found in patients over 40 years of age. The highest incidence is in the sixth decade, namely, 10 cases or 30 per cent. It

is the only type of benign growth which predominates in patients of advanced age. This is unusual, since only malignant tumors are more common in advanced years. The youngest patient was 11 years of age and the oldest 88 years of age.

Tuboovarian Cysts.—(29 cases.) Although the number of cysts is limited, the age incidence occurs as one would expect, i.e. 40 per cent or 11 cases in women between twenty and thirty years; 10 cysts, or 30 per cent, among thirty- to forty-year-old patients; and the remainder in patients between forty and fifty years. No case occurred in a patient under twenty years of age or over sixty years of age.

Fibromas.—(24 cases.) These tumors are distributed over all decades between ten and seventy years. In the fourth decade 37 per cent were found; in the sixth decade, 20 per cent; and in the third and fifth decades, an incidence for each of 17 per cent was found.

Papillary Pseudomucinous Cystadenocarcinoma.—(11 cases.) This small group of cancers is divided equally among the patients of all decades from twenty to seventy years, and corresponds roughly with the frequency of its benign form.

Embryonal Neoplasms.—(10 cases.) The 80 per cent incidence in young patients between ten and twenty years of age is striking. Six of the teratomas and both the dysgerminomas are found in this age group.

Rare Malignant Tumors.—(28 cases.) More than half of the sarcomas and carcinomas are found in patients over forty years of age; namely, 7 of the 9 sarcomas and 10 of the 19 carcinomas; the former are fibrosarcomas, hemangio- and angiosarcomas; the latter are made up of medullary, Krukenberg and solid carcinomas, as well as both the squamous cell carcinomas in dermoid cysts. In patients under twenty years, the sarcomas found were spindle, round cell, and hemangiosarcomas, and the carcinomas were 4 of the 6 Krukenberg tumors.

One carcinoma was found in the ten- to twenty-year age group and one in the sixty- to seventy-year age group. Thus, 70 per cent of the sarcomas and 67 per cent of the carcinomas were in women over forty years of age; 22 per cent of the remaining cancers were in patients between thirty and forty years.

It is obvious that ovarian sarcoma incidence is not in accord with these figures.

SUMMARY

Considering the entire group of 1,101 tumors, it is observed that 58 per cent were removed from women between the ages of twenty and forty years; (31 per cent in the fourth and 27 per cent in the third decades); 30 per cent of the tumors were found in patients over forty years, and 10 per cent under twenty years.

The predominating number of simple cysts (82 per cent), dermoid cysts (83 per cent), pseudomucinous cystadenomas (73 per cent), and endometriosis of the ovary (93 per cent) were found in the age group between twenty and fifty years.

The predominating number of papillary serous (84 per cent), and pseudomucinous cystadenocarcinoma (72 per cent), also papillary cystadenomas (72 per cent) and fibromas (74 per cent) are found in the age group between thirty and sixty years.

Thus, in the period of ovarian activity, namely, between twenty and forty years, more than half the ovarian tumors are found.

III. FREQUENCY OF OVARIAN TUMORS BY AGE GROUPS (DECADES)

The largest number of ovarian tumors is found in women between the ages of thirty and forty years; 347 cases are recorded, an incidence of 31 per cent. Simple cysts comprise 55 per cent of this number, or a total of 189 cases. Dermoid cysts, then papillary serous cystadenocarcinomas, follow in order of their frequency in this decade; namely, 16 per cent and 10 per cent.

Next in frequency is the third decade, twenty to thirty years, in which 302, or 27 per cent, of ovarian tumors were found. The 162 simple cysts representing 53 per cent of these tumors are the most frequent, then, 74 dermoid cysts, constituting 21 per cent, and 15 pseudomucinous cystadenomas, namely, 5 per cent.

Third in order of frequency is the fifth decade, forty to fifty years, in which are 216 ovarian tumors, or 19 per cent of all ovarian newgrowths. Again, simple cysts have the highest frequency, namely, 81 instances or 37 per cent. Fifty-five papillary serous cystadenocarcinomas, namely, 25 per cent, and 24 dermoid cysts, namely 11 per cent, are also noted as second and third in frequency.

The 113 tumors found in the second decade, namely, between ten and twenty years, bring this age group into fourth place in order of its ovarian tumor incidence. The simple cyst (77 cases) is the principal neoplasm in this decade, with an incidence of 68 per cent. The dermoid and pseudomucinous cystadenomas follow in order.

In the sixth decade only 93 ovarian tumors are found, namely 8.3 per cent. This age group is fifth in order. The most frequent tumor is the papillary serous cystadenocarcinoma, constituting 44 per cent or 40 instances. There was a twelve per cent incidence of papillary serous cystadenoma, namely 11 cases, and an 11 per cent incidence of simple cysts, namely, 10 cases.

Between the ages of sixty and seventy years, there were 26 cases constituting only 2.3 per cent of all ovarian tumors; forty per cent of these are represented by the 10 papillary serous cystadenocarcinomas, 20 per cent by 5 dermoid cysts and 8 per cent by 2 simple cysts.

SUMMARY

It is of interest to note that of the 786 tumors in patients between ten and fifty years, 509 or 65 per cent were simple cysts. The second outstanding tumor, the dermoid cyst, has a 21 per cent incidence (166 cases), the papillary serous cancer with 11 per cent incidence (89 cases) and the papillary pseudomucinous cancer with a 3 per cent incidence (22 cases), are third and fourth in frequency.

In 115 patients under twenty years, simple cysts predominate; there were 77 (or 67 per cent) of these. Dermoid cysts are second in frequency with an 11 per cent incidence (15 tumors).

One hundred and twenty-one or 11 per cent of all ovarian tumors are in women over fifty years; papillary serous cystadenocarcinomas comprise forty per cent (50 cases) of this group. Its benign form is second in incidence, namely 11 per cent (13 cases). Twelve simple cysts were 10 per cent of this entire age group.

III. MALIGNANT AND BENIGN TUMOR INCIDENCE IN THE ENTIRE GROUP, IN MENOPAUSE AND PREMENOPAUSE

There are 139 patients found in menopause, and 963 in the premenopause age. Eighty or 58 per cent of the former and 11.5 per cent of the latter had ovarian malignancies. Thus, a climacteric patient with an ovarian mass has a 58 per cent possibility of ovarian cancer. Eighty or 42 per cent of the 191 ovarian carcinomas in this series occurred in menopause women, and 111 or 58 per cent in premenopause women.

Fifty-eight or 6.3 per cent of the 910 benign tumors were found in menopause women and 93.7 per cent or 852 patients were in the premenopausal group.

TABLE III

	MENOPAUSE		PREMENOPAUSE		TOTAL	
All tumors	138		963		1,101	
Malignant	80	58%	111	11.5%	191	17%
Benign	58	42%	852	88.5%	910	83%

III. MALIGNANCY DURING MENOPAUSE

Sixty-two or 71 per cent of the 80 cancers removed from patients in menopause were papillary serous cystadenocarcinomas. This number comprises 43 per cent of all (152) these serous cancers.

Both squamous cell carcinomas in dermoid cysts, the single angiosarcoma and the carcinoma of undetermined type occurred in menopause patients. In this group also are found 75 per cent of fibrosarcomas, 67 per cent of solid carcinomas, 50 per cent of 6 medullary cancers and 2 hemangiosarcomas. Four of the 11 pseudomucinous cystadenocarcinomas were operated during climacterium. Only 1 of the 6 colloid cancers was removed from a menopause patient.

Spindle cell, round cell and carcinosarcoma were not found among menopause patients.

III. BENIGN TUMORS DURING MENOPAUSE

Only 6.4 per cent or 58 of the 910 benign growths were found in menopause patients. The following make up this number: 36 per cent of the 36 papillary serous cystadenomas, namely, 13 cases; eight per cent of the 64 papillary pseudomucinous cystadenomas, or 5 cases; and 7 per cent of the 182 dermoid cyst patients, namely, 13 cases. Between 2 and 3 per cent of each of the following tumors were removed from climacteric women: simple cysts, endometriosis of the ovary, and fibromas. No case of tuboovarian cyst, teratoma or disgerminoma was observed in a menopause patient.

IV. MARITAL STATUS, PARITY AND GRAVIDITIES AMONG OVARIAN TUMOR PATIENTS

Seventy-five per cent of all ovarian tumors are found in married patients and 25 per cent in single women. (670 were married and 240 were single.)

A. *Benign and Malignant Tumors in Relation to Marital Status.*—In married women are found 75 per cent (682) of the 910 benign tumors, and 81 per cent (155) of the 191 malignant tumors.

B. *Relation of Marital Status to Benign and Malignant Tumors.*—Benign tumors are found in 87 per cent (240) of the 276 single patients and 81 per cent (668) of 825 married women. Malignant tumors make up the remainder. Moench reports that 76 per cent to 89 per cent of serous benign and malignant tumors and solid cancers occur in married women.

C. *The Nature of the Tumor in Relation to Parity.*—Although 825 patients in the group were married only 355 or 43 per cent were parous. Thirty per cent of 190 malignant tumors and 32 per cent of 911 benign tumors were in parous patients, while 70 per cent of 190 malignant tumors and 68 per cent of 911 benign tumors were in nonparous women. Thus both types are twice as common in nonparous women.

D. *Parity in Relation to the Nature of the Tumor.*—Sixteen per cent of both parous and nonparous patients had ovarian cancer, while 84 per cent of each had benign tumors of the ovary. Thus, both parity and nonparity are five times more common among benign than among malignant neoplasms.

E. *Gravidities Among Ovarian Tumor Patients.*—Parity among the 825 married women is 43 per cent; among all patients regardless of marital status, 32 per cent. Among patients with dermoid cysts, simple cysts, and papillary serous cystadenocarcinomas, parity is from 28 per cent to 36 per cent. In the small groups, with the exception of fibrosarcomas, parity is from 20 per cent to 53 per cent. All disgerminomas, spindle cell sarcomas, round cell, angio- and hemangiosarcomas, as well as carcinosarcomas, occurred in nulliparous women of or past the childbearing age. Three of the 4 fibrosarcoma patients had borne children. One

child gravidity is most common: 29 per cent of parous women had one child and 25 per cent had two children. In a tuboovarian cyst patient, 20 pregnancies were reported. Moench reports between fifty per cent and 63 per cent parity in benign and malignant serous tumor patients and solid carcinomas. My figures are 40 per cent less than these. Randazzo states that 32 per cent of ovarian cyst patients are sterile.

V. UTERINE BLEEDING

Since ovarian structure in most instances in this group had undergone considerable, if not complete alteration, the high incidence of normal menses, namely, 54.3 per cent or 598 cases among 1,101 ovarian tumors is significant, especially in the light of the present facts with regard to the relationship of the ovary to the menstrual function.

Hyperfunctional ovarian bleeding occurred in 292 patients, or 26.5 per cent of all tumor cases. There were 123 of these or 11 per cent with metrorrhagia, 136 or 12.3 per cent had menorrhagia, and 3.3 per cent or 33 patients had menometrorrhagia.

Hypofunctional ovarian bleeding incidence is 17.9 per cent, representing 198 patients. Of these, 138 patients or 12.3 per cent were in the menopause. Three per cent or 38 patients complained of secondary amenorrhea, and 2 per cent or 22 patients complained of oligomenorrhea. Neither of the latter two groups can be considered climacteric in origin since these patients were all young women.

Normal Menses.—Those tumor groups showing highest incidence of normal bleeding, namely, 64 per cent in each, are the dermoid cyst and the pseudomucinous cystadenocarcinoma. Next in order is the 60 per cent incidence of a normal cycle among patients with pseudomucinous cystadenomas. Fifty-six per cent of both simple cyst patients and women with ovarian endometriosis reported normal bleeding.

The tuboovarian cyst and papillary serous cystadenocarcinoma patients show 45 per cent incidence of regular uterine bleeding, and among the papillary serous cystadenoma patients the incidence was 41 per cent.

Three of the 8 teratomas, 2 of the 6 medullary carcinomas, and one of the 6 colloid cancers, as well as one of the 4 fibrosarcoma patients, reported normal uterine bleeding.

Twenty-five per cent of 24 fibroma patients had normal bleeding. In the single instances of the following tumors there were also normal menses; namely, spindle cell sarcoma, carcinosarcoma, and solid carcinoma.

Menorrhagia.—This form of bleeding is not observed with great frequency. It appears most frequently among ovarian endometriosis cases, namely, thirty per cent incidence, among 20 per cent of the tuboovarian cysts, and in 16 per cent of the simple cyst patients.

Dermoid cysts and both benign and malignant papillary serous tumors, papillary pseudomucinous adenomas and teratomas, each show a small number of instances of menorrhagia. In a patient with purpura-hemorrhagica, menorrhagia was also noted.

Except for one round cell sarcoma patient, there is not a single instance of this type of bleeding among the rare malignancies or the embryonal tumors.

Metrorrhagia.—The highest incidence of this form of bleeding, namely 34 per cent, was found among the tuboovarian cyst patients; 14 per cent of simple cysts and nine per cent of patients with endometriosis of the ovary show this form of uterine bleeding.

It occurred in 33 per cent of the fibroma cases, in 5.2 per cent of serous papillary cancer, and in 7.7 per cent of pseudomucinous papillary cystadenoma patients.

Ten per cent of the dermoid cyst patients complained of this symptom. Among colloid (Krukenberg) and medullary cancers only a few instances are reported.

Menometrorrhagia.—This is an uncommon form of bleeding in patients with ovarian growths. Its presence is noted in only four of the groups.

Simple cyst patients show an incidence of 5.3 per cent and dermoid cysts, serous papillary cystadenocarcinomas and pseudomucinous papillary cystadenoma patients complained in about 1.5 per cent of the instances in each group.

Menopause.—One hundred and thirty-eight or 12.5 per cent of all ovarian tumors were removed from patients during menopause. Forty-two per cent or 58 of the above number of patients were operated upon for benign tumors. The incidence of menopause among the types of benign tumors is as follows: Thirty-six per cent of serous papillary cystadenomas and 21 per cent of fibromas were found in climacteric women. Only 2.5 per cent, respectively, of simple cysts and ovarian endometriosis occurred during this period. Eight per cent of both dermoid cysts and pseudomucinous papillary cystadenomas were removed from menopausal women.

Fifty-eight per cent or 80 of the 138 menopausal tumors were cancerous. Their distribution is as follows: Sixty-two or 41 per cent of the 152 serous, and 4 or 36 per cent of the 11 pseudomucinous papillary cyst adenocarcinomas were operated upon during menopause. Three of the 6 medullary cancers, 2 of the solid cancers and both of the squamous cell cancers developed in dermoid cysts were removed from patients of menopause age.

All three fibrosarcomas were in menopause patients.

Angio- and hemangiosarcoma as well as colloid cancer, in one instance each, fall in this group also.

Menopausal Uterine Bleeding.—This type of bleeding occurs only 14 times in 1,101 tumor patients, an incidence of 1.3 per cent. Two of the 522 simple cyst patients, namely, 0.4 per cent; 6 of the 152 papillary serous carcinomas, namely, 4 per cent; and 2 of the 4 fibrosarcoma patients, namely, 50 per cent, are in this group. This condition is also noted in one of the colloid cancer patients, as well as in a case of ovarian fibroma and in a patient with medullary carcinoma of the ovary.

Amenorrhea.—Thirty-eight patients of menstruating age had amenorrhea, an incidence of 3 per cent. 12.8 per cent of the pseudomucinous papillary adenomas (8 of 64 cases), 5 per cent of the dermoid cyst patients (9 of 182 women), and 3 per cent of the simple cyst cases (15 of 522 patients), had amenorrhea.

Other Menstrual Irregularities.—Other forms of abnormal bleeding do not appear frequently enough to warrant more than passing mention. In one of the patients with teratoma of the ovary, purpura hemorrhagica was noted with menorrhagia.

Primary amenorrhea occurred in two of the young patients with teratoma and also in a sixteen-year-old girl with bilateral fibromas of the ovary. Clinically, in the latter case, a mannish voice and stature, and hypertrichosis were observed. The tumors were grapefruit and lemon size, respectively, and had undergone calcific and fatty degeneration.

Oligomenorrhea, interval staining, spotting as in ectopic pregnancy, and prepuberty bleeding occurred uncommonly and without particular frequency in any tumor type. Four instances of the latter type of bleeding (prepuberty bleeding) among young patients with dermoid cysts are of interest.

The wide variety of vaginal bleeding coincidentally found with 1101 ovarian tumors indicates that the diagnostic importance of this symptom cannot be stressed. The preponderance of the normal menses over all other bleeding forms, in spite of the partial or complete anatomical ovarian change, is striking.

It may be concluded that structural ovarian change appears to have no relation to the functional activity of the ovary.

VI. DYSMENORRHEA

There were 131 instances of this symptom among 858 cases; the latter figure excludes patients amenorrheic because of menopause, oligomenorrhea and other causes. The average total incidence of this symptom is 15 per cent. (Table IV.)

Dysmenorrhea is found with endometriosis of the ovary in 21 per cent of 42 patients. Simple cysts show 19 per cent incidence and papillary serous and pseudomucinous cystadenomas show a 12 per cent and 13 per cent frequency, respectively, whereas 14 per cent is observed in malignant pseudomucinous cystadenocarcinomas.

TABLE IV. DYSMENORRHEA

TYPE	NO. OF PATIENTS	DYSMEN-ORRHEA	PER CENT OF TOTAL
Simple cysts	478	94	19.4
Dermoid cysts	156	15	9.5
Papillary serous cystadenocarcinoma	82	3	3.6
Papillary pseudomucinous cystadenoma	19	6	12.0
Endometriosis of the ovary	42	9	21.0
Papillary serous cystadenoma	22	3	13.0
Papillary pseudomucinous cystadenocarcinoma	7	1	14.0
Tuboovarian cysts	29	0	0
Fibroma	23	0	0
Total	858	131	15.0

VII. METASTASES IN MALIGNANT OVARIAN TUMORS (TABLE V)

At operation 76 per cent of 190 patients with ovarian malignancy were found to already have metastases; 412 separate foci were noted. In many patients there were numerous sites of spread. Metastases was not found with round cell and angiosarcoma.

A. *Incidence by Body System.*—The greatest number of areas of metastases was found in the *gastrointestinal* tract and *peritoneum*, namely, 105 in each, or 26 per cent of all foci of spread.

There are 79 instances of gastrointestinal tract invasion from 152 papillary serous cancer, 14 instances by 6 colloid or Krukenberg tumors, 5 instances by 6 medullary carcinomas, and 4 instances by 11 papillary pseudomucinous cystadenocarcinomas. Among 2 squamous cell carcinomas in dermoid cysts the intestinal tract was involved once, and in the 2 hemangiosarcomas, 2 intestinal foci of spread were found.

Eighty-seven instances or 57 per cent of peritoneal invasion were noted in the 152 papillary serous cystadenocarcinomas, 5 instances or 45 per cent among the

TABLE V. INCIDENCE OF THE METASTATIC FOCI IN 190 OVARIAN CANCERS

SITE	NUMBER	
Peritoneum	106	26%
Gastrointestinal tract	105	26%
Gynecologic system	66	16%
Omentum	47	11%
Other organs	34	9%
Lymphatic tract	23	5%
Genitourinary tract	18	4%
Respiratory tract	13	3%
Total number of metastatic foci 412		

11 papillary pseudomucinous cystadenocarcinomas, and 4 peritoneal metastases each were noted in both colloid and medullary cancers. Carcinosarcoma, solid carcinoma and squamous cell carcinoma in a dermoid cyst each account for one instance of peritoneal spread, while in both hemangiosarcoma patients the peritoneum was also involved.

The *gynecological tract* contains 66 of the 412 foci or 16 per cent: The tumor accounting for 57 of the 66 instances is the papillary serous cystadenocarcinoma. The most frequent structure involved is the uterus; next in frequency are the homolateral tube and contralateral ovary. The contralateral tube and broad ligaments contain metastases of slightly less frequency.

The pseudomucinous cystadenocarcinoma accounts for 2 uterine foci. The colloid cancers show spread to the tube and broad ligament and infundibulo pelvic ligament, and the medullary cancer shows spread to the broad ligament in 3 instances and also to an inguinal hernia sac.

Other involved structures are mesosalpinx, ovarian cortex, rectovaginal septum, vaginal wall and fornix, cervical stump and parametrium.

The *omentum* revealed 47 foci or 11 per cent of all sites of spread. Thirty-five of the 47 instances of omental involvement were papillary serous cyst adenocarcinoma. There were 3 instances each among papillary pseudomucinous cyst adenocarcinomas and colloid cancer, and 4 among 6 medullary carcinomas. In one of the squamous cell carcinomas in dermoid cyst and in one hemangiosarcoma patient, the omentum was also involved with metastasis.

Various organs reveal 34 carcinomatous metastases, an incidence of 9 per cent, 15 of the 20 liver metastases, 4 abdominal wall foci and malignant spread to breast, adrenal, spleen and subcutaneous originated from papillary serous cystadenocarcinomas. The liver was involved also by pseudomucinous carcinoma, spindle cell and hemangiosarcoma. Colloid and medullary cancers showed spread to the umbilicus and also to the spleen and an abdominal scar.

Although malignancy spreads through the *lymphatic stream*, only 23 instances of cancer were found, an incidence of 5 per cent. The iliac, abdominal, periportal, mediastinal, aortic, perirenal, axillary and gastric lymphatics were invaded in all instances from the papillary serous cystadenocarcinomas. Four of the 13 metastatic pelvic node cancers arose from the pseudomucinous and 7 from the serous papillary cystadenocarcinomas. Two pelvic node metastases took origin from the squamous cell carcinomas in dermoid cysts.

The *genitourinary tract* contained 18 cancerous foci, or 4 per cent of the total number: The bladder was involved 9 times in all; six times from serous papillary malignancies, one from a colloid, and one from a medullary carcinoma. An angiosarcoma was the origin of another.

Patients with squamous cell carcinoma in a dermoid cyst, medullary carcinoma, and papillary serous cystadenocarcinoma had both unilateral and bilateral ureteral metastases.

There was one case of pyonephrosis in a serous ovarian cancer. Ureteral orifices were involved twice by papillary serous cystadenocarcinoma and in a third patient with this tumor the vesicocervical junction was completely invaded.

The *respiratory tract* accounts for 13 cancerous foci or 3 per cent. Papillary serous cystadenocarcinomas were the origin of metastases to the right lung in 5 cases and to the pleura and diaphragm in 4 instances each. Pleural effusion was noted in 5 patients, each of whom had papillary serous cystadenocarcinoma of the ovary. The incidence of this finding is 2.7 per cent in the 190 patients. The respiratory tract accounts for 3.1 per cent of all metastatic foci from ovarian cancer.

B. Incidence in Single Structures.—Of the single structures involved by metastases, pelvic peritoneum has the highest incidence, namely, 73 instances or 17 per cent. The omentum, discussed above, is second; culdesac was involved separately in 13

patients. The small intestines (30) and sigmoid (27) contained 7.2 per cent and 6.5 per cent of metastatic foci, respectively; 5.8 per cent or 24 instances of rectal metastases were observed. Liver and abdominal peritoneum were invaded 20 times each, or 4.8 per cent. In 15 instances, uterine spread was noted, and 10 foci in retroperitoneal nodes were found.

Abdominal carcinomatoses and "frozen" carcinomatous pelvis were observed in 12 patients, respectively. Structures involved also were stomach, duodenum, bladder, ureter, and lung, pleura and diaphragm. The vagina, cervical stump, rectovaginal septum as well as spleen, adrenals, breast, pericardium and mesentery, were sites of metastasis from ovarian cancer. Nodules were demonstrable also in the umbilicus, in abdominal scars and in an inguinal hernia sac.

Retroperitoneal pelvic lymphatics were invaded in 13 instances; iliac and abdominal groups in two patients. Involvement of the periportal, mediastinal, aortic, perirenal axillary and gastric nodes is evidence of the invasive character of carcinomas of the ovary.

C. Metastasis in Each Cancer Group.—One hundred forty-four of the 190 malignant tumors were found, upon laparotomy, to have invaded either surrounding or distant body structures. This high incidence of 76 per cent is an indication that symptoms are either very mild or occur too late in the disease for a reasonable possibility of operative cure. Many patients present themselves in a stage of carcinomatosis peritonei, with symptoms of but two to three months duration!

Seventy-seven per cent of the 152 serous, and 73 per cent of the 11 pseudomucinous papillary cystadenocarcinoma tumors had already invaded secondary structures before surgical treatment could be employed.

All of the 6 Krukenberg cancers, and 83 per cent of the 6 medullary tumors had spread before these patients were treated surgically.

Both hemangiosarcomas and the single cases of spindle cell and carcinosarcoma had metastatic foci when laparotomy was performed.

The fibrosarcoma, the solid sarcoma, and the squamous cell carcinoma in a dermoid cyst had metastasized in 25 to 50 per cent of the patients.

The single angio- and round-cell sarcoma showed no metastasis.

D. Ascites in 190 Ovarian Malignancies.—Fifty-four per cent (or 103) of malignancies were found with intraabdominal or pelvic fluid. (Lippert's incidence for ascites is 78 per cent and Moench reports 79 instances in 274 ovarian malignancies or 32 per cent.)

Clear, bloody, or purulent fluid was common to all malignant tumors. Seventy-one per cent of instances with ascites had clear fluid, 22 per cent, bloody, and 7 per cent purulent fluid.

Ninety-five per cent of ascites was due to papillary serous cystadenocarcinoma, which predominates also in all the above types of ascitic fluid.

Of 152 papillary serous carcinomas, 95 or 62 per cent had ascites; of the 11 pseudomucinous cancers, 3 or 27 per cent, and of the 12 medullary and colloid tumors, 4 or 33 per cent, had ascites; one of the 4 fibroma cases had free fluid. (Zangmeister reports ascites in 29 of 36 fibromas [Kaufmann Path. p. 1581, v. 2] and Pfannenstiel a 25 per cent incidence for ascites for these growths.)

VIII. SYMPTOMS AND SIGNS IN PATIENTS WITH OVARIAN TUMORS

A total of 1814 symptoms was noted in the histories of all patients (1101) with ovarian tumors, among which are 900 benign and 163 malignant growths. Symptoms are classified as pain, gastrointestinal, abdominal, bladder, respiratory, and miscellaneous. A comparison between symptoms due to benign and malignant tumors is made,

Most complaints were mild in character and their insidious onset accounts for late recognition of disease. Symptomatology was not always referable to the pelvis and therefore many patients reached the gynecologist late in the course of disease.

Pain.—Pain constitutes 44 per cent of all symptoms; 75 per cent of all the patients, namely 802, had pain; 11 per cent of this symptom is found among 91 malignant, and 89 per cent among 711 patients with benign tumors. It may also be noted that 91, or 55 per cent, of all malignant and 711, or 79 per cent of all benign tumor patients complained of pain. Pain is slightly more frequent in benign growths.

Seventy-five per cent of simple cysts, 95 per cent of dermoid cysts, and 65 per cent of papillary pseudomucinous cystadenomas produced pain. Ninety-three per cent of patients with endometriosis of the ovary, 75 per cent of papillary serous cystadenoma patients, 76 per cent of tuboovarian cyst patients, and 58 per cent of fibromas also suffered from pain. Fifty-six per cent of papillary serous and 45 per cent of papillary pseudomucinous cancer patients complained of pain. (Moench states that 52.6 per cent of 274 patients had pain.)

Thus, pain is a fairly constant feature, but it is either so mild in its nature or so delayed in its onset that its importance in early diagnosis is greatly diminished.

Gastrointestinal Symptoms.—There are 358 or 19 per cent of 1814 symptoms in this group. Seventy-four instances or 20 per cent of these complaints are found in malignancy patients and 284 or 80 per cent in the benign growth patients. There are 74 symptoms among the 163 malignancy cases, a 45 per cent incidence. The 900 benign tumors show an incidence of 27 per cent. Thus, these symptoms occur one and a half times more frequently in patients with malignant tumors.

Vomiting and nausea are the principal complaints, representing 33 per cent and 26 per cent, respectively, of all intestinal symptoms. Thirteen per cent of these instances occurred in malignant tumor patients. Constipation, cramps, and dyspepsia are frequent symptoms. Four and four-tenths per cent of all intestinal symptoms are caused by bowel obstruction and 88 per cent of these were in malignant patients. Rectal complaints, few in number, were manifest only in carcinoma patients.

Abdominal Signs.—Two hundred ninety-five, or 16 per cent of the 1814 complaints comprise this group; 28 per cent of these were in malignancy patients; 235 instances of abdominal mass represent 80 per cent of these complaints; 35 per cent of patients with abdominal mass had ovarian cancer. Abdominal rigidity (17 per cent of this group) was found in 50 patients with simple cysts.

Bladder Symptoms.—One hundred thirty-eight symptoms represent only 8 per cent of all the complaints. Malignancy patients account for 32 per cent of bladder symptoms. Dysuria, urinary frequency, and urgency occur in this order of incidence. Dysuria comprises over 50 per cent of bladder symptoms.

TABLE VI. SUMMATION OF SYMPTOMS AND SIGNS IN BENIGN AND MALIGNANT TUMORS

SYMPTOMS	MALIGNANT TUMOR PATIENTS		BENIGN TUMOR PATIENTS		TOTAL NO. 1,063
	163	PER CENT	900	PER CENT	
Pain	91	11	711	89	802
Gastrointestinal	74	20	284	80	358
Abdominal signs	85	28	210	72	295
Bladder symptoms	44	32	94	68	138
Respiratory symptoms	4	57	3	43	7
General symptoms	79	36	135	64	214
	377	20	1,437	80	1,814

Respiratory Symptoms.—Cough, dyspnea, and hemoptysis are complaints infrequently heard. They are noted only among carcinoma patients. Pleural effusion was demonstrated in a case of pseudomucinous cystadenocarcinoma.

General Symptoms and Signs.—Fainting, vertigo, shock, headache, and nervousness comprise 18 per cent of this group. Chills and fever are infrequently noted. Twenty-eight sterility complaints were found in simple and dermoid cyst patients. Hypertrichosis and mannish voice were found in a patient with fibroma of the ovary.

IX. SITE OF PAIN AND POSITION OF OVARIAN TUMORS

(a) *Sites of Pain* (802 cases): This symptom occurred in 75 per cent or 802 of all the patients. In the remaining 25 per cent, pain was either not mentioned or not recorded. A fair concept of the correlation between the sites of pain and pathology is obtained by comparing the percentage incidence of each.

Pain in the right, left or bilateral lower quadrants is a complaint in 70 per cent of these women; the remaining 30 per cent is made up of various other body areas, not directly referable to the pelvis.

Twenty-seven per cent and 25 per cent of the complaints, respectively, were referable to the right and left lower quadrants, while 18 per cent were bilateral. Thus, unilateral is about three times more frequent than bilateral pain. Back and abdominal complaints are not infrequent. Suprapubic, epigastric and thigh pains occur often, while right upper quadrant, umbilical and left shoulder pains are rare.

(b) *Position of All Tumors* (1,063 cases): In this series, 21 per cent of all ovarian tumors were bilateral.

My figures of right (44 per cent) and left side (35 per cent) incidence are similar to those of other authors. The right side incidence is slightly greater. One per cent of ovarian tumors in this series is intraligamentous.

Position of Malignant and Benign Tumors.—Bilaterality occurs in 55 per cent of all malignancies. The incidence of bilaterality among sarcomas is 10 per cent. Papillary serous cystadenocarcinomas show 57 per cent bilaterality. Solid carcinomas are found bilateral in 10 per cent in this series.

Among the *benign tumors*, simple cysts are bilateral in 15 per cent of instances. Dermoid cysts are bilateral in 11 per cent of cases. Papillary serous cystadenomas are found bilaterally in this series in 22 per cent, by Frank-Feresten in 12.7 per cent, and by Pfannensteil in 60 per cent of cases. Six per cent of papillary pseudomucinous cystadenomas are bilateral. Fibromas appear bilateral in 15 per cent of cases: in the Frank-Feresten series, 29.4 per cent is reported and Hoon reports 3.6 per cent.

SUMMARY

From the total figures in table VII, it is noted that (a) unilateral pain is three times more frequent than bilateral pain, while the unilateral tumor is four times more frequent than the bilateral; that (b) only 27 per cent of the sites of pain were

TABLE VII. CORRELATION BETWEEN THE PAIN SITE AND THE SITE OF THE PATHOLOGY IN 802 PATIENTS

	R.L.Q.	L.L.Q.	BILATERAL	BACK, ABDOMEN, SHOULDER, R.U.Q., THIGH, ETC.
Pain location in 802 cases	27%	25%	18%	29%
Tumor location in 1,063 cases	44%	35%	21%	0
Per cent incidence of correlation between pain and pathology site	61%	70%	86%	0

in the right lower quadrant and 44 per cent of the tumors were on that side; that (e) only 25 per cent of pain sites were in the left lower quadrant, while 35 per cent of the tumors were on that side; that (d) 18 per cent of pain area was bilateral and here the pathology was bilateral in 21 per cent of cases.

Thus, 61 per cent of the right side and 70 per cent of left side tumors cause homolateral pain, while 80 per cent of bilateral tumors are accompanied by bilateral pelvic pain.

The greatest coincidence of pain sites and pathology is noted among bilateral ovarian tumors.

X. SEDIMENTATION TEST

This test was performed 298 times for the 1101 patients or 27 per cent of all cases. The recent clinical use of the test accounts for the small number of instances presented. There were 71 patients with rapid sinking time indicating infection; 60 per cent or 180 showed a rate between thirty and sixty minutes, and the remainder 16 per cent or 47 patients showed a response over 60 minutes and as prolonged as 340 minutes.

The significance of sedimentation rate is of importance in inflammatory adnexal conditions, in degenerations of benign and malignant tumors, and in infections superimposed upon twisted or infarcted ovarian tumors.

Sixty per cent of simple cyst patients showed a sedimentation rate between thirty and sixty minutes and 14 per cent less than thirty minutes; twenty-five per cent of them were over one hour. Sixty per cent of the cases in which papillary serous cyst adenocarcinoma was found had sedimentation rates under thirty minutes; 41 per cent were between thirty and sixty minutes. Fourteen per cent of patients with dermoid cysts had rapid sedimentation rates; 66 per cent were over thirty minutes and 12 per cent were over sixty minutes.

Sixty per cent of tuboovarian cyst patients had a sedimentation rate between thirty and sixty minutes; 40 per cent were under thirty minutes. However, only 3 per cent of this small group of tumor cases, namely, 10 patients, were tested.

CONCLUSIONS

1. A single complete analysis of clinical and pathologic data from a large number of ovarian tumor operations is warranted, since no such report appears in the literature. The facts, of interest to the surgeon and clinician, justify publication.

2. *Frequency*: The simple and dermoid cysts are first and second in order of incidence. Papillary serous cancer occupies a position of hitherto unreported high frequency, namely third; it constitutes 80 per cent of all ovarian cancers, and is 4 times more frequent than its benign form. It is 14 times more frequent than the pseudomucinous cancer of the ovary.

3. *Malignancy Incidence*: 17.3 per cent of all ovarian tumors are malignant; 95 per cent of these are cancer and 5 per cent sarcoma.

4. *Age Incidence*: 58 per cent of all ovarian tumors are in patients between twenty and forty years; 30 per cent are over forty years and 12 per cent under twenty years.

Sixty-seven per cent of cancer and 70 per cent of sarcoma were in women over forty years; 22 per cent of cancer was in patients between twenty and thirty years. Sixty per cent of benign serous tumors are in patients over forty years.

The fourth decade contains 31 per cent of ovarian tumors, the third decade 27 per cent and the fifth decade, 19 per cent. Simple cysts predominate in all three decades.

5. *Marital Status and Parity*: 75 per cent of tumors of the ovary are found in married patients; 81 per cent are benign and 19 per cent malignant; 43 per cent of married women with ovarian growths were parous; 30 per cent of malignant tumors were in parous women.

6. *Menses*: Normal menses occur in 54.3 per cent of patients with ovarian tumors; hyperfunctional bleeding in 26.5 per cent and hypofunctional bleeding in 17.9 per cent.

In view of the present knowledge with regard to the ovarian effect on menstruation, the high incidence of normal menses is notable.

Eleven per cent metrorrhagia, 12.3 per cent menorrhagia, and 3.3 per cent menometrorrhagia; and 12.3 per cent menopause, 3 per cent secondary amenorrhea, and 2 per cent oligomenorrhea, are the figures obtained.

In 58 per cent of menopause patients malignancies were found. Thus a climacteric patient with an ovarian tumor has a 58 per cent possibility for cancer. Eighty per cent of all malignancy occurs in menopause women.

7. *Dysmenorrhea*: The incidence of this symptom was only 15 per cent.

8. *Metastases* are noted at operation in 76 per cent of ovarian cancer patients; 80 per cent of these are due to papillary serous cystadenocarcinoma. The insidious character of an ovarian malignancy is indicated by this figure, as well as the difficulty in an early diagnosis.

Twenty-six per cent of metastases are found in the gastrointestinal and peritoneal systems. The gynecologic tract and omentum contain 16 per cent and 11 per cent, respectively. Lymphatics, genitourinary and respiratory systems, and various organs are found to have the remainder of foci.

Ascites incidence is 54 per cent in malignancy; 95 per cent of this finding is caused by papillary serous cystadenocarcinoma; 71 per cent have clear fluid, 22 per cent bloody, and 7 per cent purulent fluid.

9. *Symptoms*: Pain constitutes 44 per cent of all symptoms; 75 per cent of ovarian tumor patients have this complaint. It is not usually severe even in the late stages of carcinoma of the ovary, and is 25 per cent more frequent among the benign tumor cases.

Gastrointestinal symptoms, principally nausea and vomiting, constitute only 19 per cent of complaints; 80 per cent of these occur among the benign tumor patients; 88 per cent of intestinal obstruction is produced by cancer.

Sixteen per cent of all symptoms and signs, totaling 1814, are represented by abdominal manifestations; 72 per cent are in benign tumors. Twenty-one per cent of patients had an abdominal mass, 35 per cent of which was attributed to cancer.

Respiratory symptoms are due only to the cancer metastases, and bladder complaints are caused by benign tumors in 68 per cent of instances.

Eighty per cent of all signs and symptoms are due to benign tumors.

10. *Site of Pain and Tumors*: Seventy per cent of pain was in either the right, left, or bilateral lower quadrants; 18 per cent was bilateral, the remainder was divided equally among the right and left lower quadrants. Twenty-one per cent of tumors are bilateral, 44 per cent right and 35 per cent left; 55 per cent of malignant tumors are bilateral.

Thus, 61 per cent of right side and 70 per cent of left side tumors cause homolateral pain, while 80 per cent of bilateral tumors cause bilateral pain.

11. *Sedimentation Time*: The significance of this test is stressed in inflammatory, degenerative, and infective processes.

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2 EAST EIGHTY-FIFTH STREET

MENSTRUAL BLEEDING AFTER CORPUS LUTEUM EXCISION, FOLLOWED BY ESTRIN OR PROGESTIN THERAPY*

REPORT OF 13 CASES

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THE relative rôles of estrin and progestin in experimental menstrual bleeding monkeys were reported previously (Smith and Engle, 1932, Engle, Smith, and Shelesnyak 1935). These observations were confirmed and additional data added by Corner (1935) and Hisaw (1935).

During this period Kaufmann (1932, 1934) and others demonstrated that not only the proliferative phase of the endometrium could be produced in ovariectomized women by estrin, but also the secretory phase by estrin followed by progestin.

In the experiments on monkeys, it was shown that the uterine bleeding which follows cessation of estrin treatment could be inhibited by

*Aided by a grant from the National Research Council Committee for Research in Problems of Sex.

progestin administration, the bleeding being held in abeyance for the duration of the progestin treatment. When progestin treatment was stopped menstruation began in five or six days. After a secretory or pro gravid endometrium was developed by the use of progestin, the institution of estrin injections did not postpone or prevent the expected

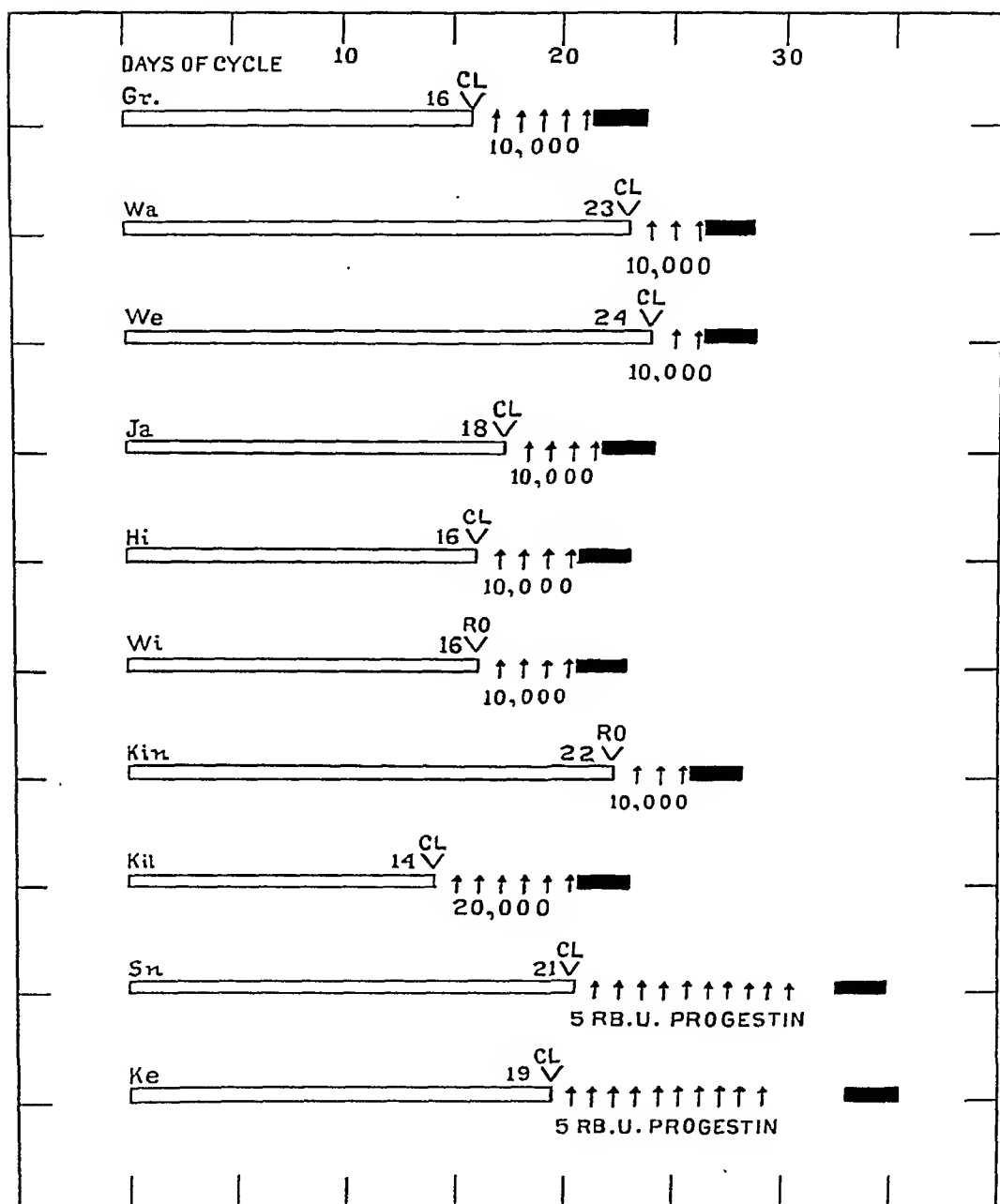


Fig. 1.—Graphic representations of uterine bleeding after corpus luteum ablation, followed by estrin or progestin treatment.

bleeding following progestin withdrawal. Estrin thus has no power to check an experimental menstrual period in the monkey in the presence of a pro gravid endometrium.

The present report extends these observations to women, and supplies additional evidence as to the rôle of the human corpus luteum in

TABLE I

NUMBER OF CASES	NAME	DIAGNOSIS	TYPE OF PERIOD	TYPE OF OPERATION	TIME AFTER ONSET OF L.M.P.	STARTED TO BLEED AFTER EXCISION OF CORPUS LUTEUM	ESTRIN DAILY R.U.	TOTAL AMOUNT R.U.
1	Gr	Fibroids	28 x 2	Excision of fibroids	16 days	Day 5	10,000	50,000
2	Wa	Fibroids	28 x 3	Excision of one fibroid	23 days	Day 3	10,000	30,000
3	We	Retroversion	28 x 4 - 5	Suspension	24 days	Day 2	10,000	20,000
4	Ja	Myoma uteri	28 x 5 - 6	Myomectomy	18 days	Day 4	10,000	40,000
5	Hi	Retroversion	28 x 3 - 4	Suspension	16 days	Day 5	10,000	50,000
6	Wi	Salpingo-oophorectomy	28 x 7	Right ovariectomy	16 days	Day 4	10,000	40,000
7	Ki	Salpingo-oophorectomy	28 x 8 - 9	Right ovariectomy	22 days	Day 3	10,000	30,000
8	Kil	Retroversion	28 x 5	Suspension	14 days	Day 6	20,000	120,000
Progestin daily								
9	Pa	Left ovarian cyst	28 x 4	Ovariectomy	28 days	Day 2	2 c.c. = $\frac{1}{2}$ Rb. U.	1 Rb. U.
10	Te	Fibromyoma	28 x 5 - 7	Myomectomy	21 days	Day 4	2 c.c. = $\frac{1}{2}$ Rb. U.	2 Rb. U.
11	Wa	Prolapse of uterus, postpartum	28 x 6	Hysteropexy	20 days	Day 3	2 c.c. = $\frac{1}{2}$ Rb. U.	1 $\frac{1}{2}$ Rb. U.
12	Sn	Cystocele-rectocele. Retroflexio uteri	31 x 3 - 5	Pelvic floor repair— suspension	21 days	Day 12	5 c.c. = 5 Rb. U.	50 Rb. U.
13	Ko	Cystocele-rectocele. Retroflexio uteri	26 x 4	Pelvic floor repair— suspension	19 days	Day 14	5 c.c. = 5 Rb. U.	50 Rb. U.

the menstrual cycle. The patients were carefully selected from hospital admissions. An attempt was made to take patients who reported fairly regular cycles. Although it is recognized that the "regular twenty-eight-day" cycle is more of a tradition than a reality, in the absence of more exact data the cases are so reported in the table summaries. The women were between the ages of twenty-five and thirty-eight years. Pelvic operations were necessary and the date of the operation was fixed at a desired time after the expected ovulation. Of these selected cases, those are reported which were found to have a fresh corpus luteum of ovulation. During the course of the operation this corpus luteum was removed.

Following this ablation of the corpus luteum, two types of treatment were given. In the first series, the patients were treated with estrin (progynon benzoate),* receiving with one exception 10,000 rat units (50,000 international units) daily. Characteristic menstrual flow began after a lapse of two to five days after excision of the corpus luteum, thus taking place before the time of the next expected period. In one case a dosage of 20,000 rat units (100,000 international units) was given daily. Bleeding began on the sixth day following excision of the corpus luteum. Thus, in these cases, as in the experiments on monkeys, estrin did not inhibit bleeding from a secretory endometrium.

In the second series, progestin† instead of estrin injections were begun at time that the corpus luteum was excised.

In the first three of these cases, an inadequate dosage of progestin was given (0.5 Rb. U. daily) and bleeding occurred on the second, third, and fourth days, respectively, after the removal of the corpus luteum. In two subsequent cases, a much larger dosage of progestin was given (Table I), and bleeding was held in abeyance beyond the next expected period. After ten days of replacement therapy, eleven days after the removal of the corpus luteum, endometrial biopsies were taken. A secretory endometrium was found. Typical bleeding occurred two and four days after cessation of progestin therapy. In one of these cases, No. 13, the patient gave a history of dysmenorrhea. At about the expected time of bleeding, she reported severe cramps and the subjective feelings of imminent menstruation. Treatment was continued for three days further but no spotting occurred. Bleeding began four days after the last day of the injections, seven days after the subjective symptoms of expectance. This was a longer cycle than this patient had reported before the operation.

SUMMARY

The clinical cases herein reported confirm for the human being the observations made on the monkeys in regard to the rôle of estrin and

*We are indebted to Dr. Erwin Schenk of Schering-Kahlbaum and Co., for furnishing part of the progynon B for these studies.
†Progestin (Organon), 1 c.c.=1 International Unit.

progestin in menstruation. Estrin, even in massive doses, does not prevent menstrual bleeding in the presence of a pro gravid endometrium if the corpus luteum is ablated. Bleeding may be inhibited after removal of a corpus luteum, for the duration of the treatment by an adequate amount of progestin. Bleeding in these cases occurs shortly after cessation of the progestin treatment, which in our cases was some days after the next expected period.

The authors wish to express their appreciation of the cooperation and interest of Dr. B. P. Watson, Director, Sloane Hospital for Women, who has made these observations possible.

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TWISTED HEMATOSALPINX COMPLICATING PREGNANCY

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MEDICAL literature is replete with references to torsion of normal and pathologic fallopian tubes, both before and after puberty, but relatively few cases of torsion of these tubes occurring during pregnancy have been recorded. This paper is concerned with a review of the cases of torsion of hematosalpinx complicating pregnancy, and with a report of one such case recently seen in our own clinic. All cases of hematosalpinx caused by ectopic pregnancy have been excluded. Since our case contributes nothing additional to the various controversies concerning such questions as torsion of normal versus torsion of abnormal tubes; the formation of hydrosalpinx before hematosalpinx; and the mechanisms of torsion, it is felt that it would be of no value to recount the discussion in the literature on these points.

After a careful search only 13 cases of twisted hematosalpinx complicating pregnancy could be found. These are summarized in Table I. In addition to these, several other cases are mentioned even though our original criteria would exclude them from this group.

Peraire¹¹ reported a case of torsion of hydrosalpinx without hematosalpinx. In the cases of Schoenholz¹⁶ and Routh,¹⁵ the tube was not twisted and collections of blood in the involved tubes were found. Hubrich⁷ reports an interesting case of intrauterine pregnancy complicated by a twisted hematosalpinx due to an old tubal abortion. Sheldon¹⁷ reports a case of complete torsion of the right tube and ovary complicating a three months' pregnancy, but does not directly state that hematosalpinx was present. This particular patient aborted on her third postoperative day.

CASE REPORT

Mrs. H. M., a white nineteen-year-old primigravida, entered the University Hospital Nov. 24, 1935, complaining of pain in the right lower abdominal quadrant associated with nausea and vomiting. It was noted upon admission that the patient was about thirty-eight weeks pregnant.

The family history was negative. In the past year's history, the patient described vague irregular pains in the lower right quadrant of the abdomen, and these episodes

TABLE I

AUTHOR	YEAR	DURATION OF PREGNANCY	AGE OF PATIENT	SYMPTOMS	PREOPERATIVE DIAGNOSIS	SIDE INVOLVED	OVARY INVOLVED	SIZE OF TUMOR	EFFECT OF OPERATION ON PREGNANCY	REMARKS
1. Hartmann ⁶	1898	5-6 mo.	20	Pain, vomiting, distention	Peritonitis	R	Yes	Not stated	Went to term	
2. Praeger ¹⁴	1899	4 mo.	35	Pain, constipation, urinary retention	Ovarian cyst on twisted pedicle	L	No	10 by 10 by 7 cm.	Not interrupted	
3. Pinard and Paquy ¹³	1901	4 mo.	26	Pain, nausea, vomiting, distention, icterus	Ovarian cyst on twisted pedicle	R	Ovary enlarged	8 by 4 by 3 cm.	Went to term	
4. Pinard ¹²	1902	Term	36	Pain, nausea, vomiting, distention	Not stated	R	No	Size of orange		Operation 6 hr. after delivery. Mother recovered
5. Aulhorn ²	1910	3 mo.	19	Pain, rigidity	Pyosalpinx	R	Swollen	9 cm.	Simply states, "recovery,"	
6. Ward ²¹	1910	4 mo.	20	Pain, nausea, vomiting, rigidity, fever	Acute appendicitis	R	Not stated	Filled abdomen	Went to term	

TABLE I—CONT'D

7. Lecane ⁸	1912	5 mo.	21	Pain, nausea, vomiting, tenderness, rigidity	Appendicitis	R	No	Not stated	"Recovery"	
8. Eastman ⁴	1927	7½ mo.	23	Pain, nausea, vomiting, tenderness	Acute appendicitis	R	Yes	"Massive"	Went to term	
9. Dellis	1928	7 mo.	24	Pain, nausea, vomiting	Appendicitis	R	No	"Large"	Went to term	
10. Green-Armytage ⁵	1929	6 mo.	16	Pain	Acute appendicitis	R	Yes	6½ cm.	Went to term	
11. Stevens ¹⁹	1930	8½ mo.	33	Pain, nausea, vomiting, tenderness	Acute appendicitis	R	Not stated	"Hen's egg"	Cesarean section at time of operation	Live baby. Mother recovered
12. McKerrow ¹⁰	1934	6 mo.	30	Pain, tenderness	Not stated	R	Not stated	"Infant's fist"	Went to term	
13. Taubenhause ²⁰	1934	3 mo.	34	Pain, nausea, vomiting	Ovarian cyst on twisted pedicle	L	No	"Hen's egg"	Therapeutic abortion 13 days after operation	Patient recovered
14. Savage	1935	38 wk.	19	Pain, nausea, vomiting, tenderness, rigidity	Acute appendicitis	R	No	7 by 6 by 6 cm.	Went to term	

had been thought by her physician to be mild attacks of appendicitis. The menses began at thirteen years of age and had always been regular and normal in every respect. There was no history of vaginal discharge or other symptoms of gynecologic importance. The last menstrual period had occurred on Feb. 25, 1935, and the estimated date of confinement was Dec. 4, 1935.

The pregnancy had been entirely uneventful until one week previous to admission when the patient experienced a sudden, moderately severe pain in the right side of the lower abdomen accompanied by nausea and vomiting. The patient was confined to her bed most of this week with remissions and exacerbations of these symptoms. On Nov. 23, 1935, there was a sudden intense pain in the right lower quadrant of the abdomen with marked increase in the nausea and vomiting. A white blood cell count at this time showed 11,000 cells per c.mm. of blood, and expectant treatment was followed. Since there was no improvement by the following day, hospitalization was advised and accepted.

Upon admission the patient was seen to be about thirty-eight weeks pregnant with the uterine fundus 30 cm. above the symphysis pubis. Her expression reflected pain and anxiety, and she was slightly more comfortable with the right thigh flexed upon the abdomen. Her face was flushed; respirations were 28 per minute; the pulse was 100 per minute; and the temperature 99° F. General physical examination was negative except for the abdominal findings as follows: the uterus was normal for a pregnant uterus, in size, shape, and consistency and was not tender; the fetus was found to be presenting L.O.T., the fetal heart was normal; and there were marked tenderness, rigidity, and muscle spasm most marked at a point in the right midaxillary line where this line would be bisected by a line drawn transversely about 3 cm. above the umbilicus.

Laboratory findings on admission were: a normal blood picture except for an increase in white blood cells to 17,000 per c.mm., and a 90 per cent concentration of polymorphonuclear cells; sedimentation rate was moderately increased; and two catheterized specimens of urine were entirely negative. A tentative diagnosis of acute appendicitis complicating pregnancy was made, although the possibility of torsion of an ovarian cyst on its pedicle was considered, and immediate operation was advised and accepted.

Upon opening the abdomen through a high right McBurney incision, a small amount of cloudy serous fluid was expressed, and a reddish purple, firm, and somewhat friable mass the size of an orange was encountered. This mass was seen to be the dilated distal portion of the right tube twisted clockwise once with the point of torsion about 2 cm. from the uterine end, and it was removed in the usual manner. The right ovary was normal in every respect and was not removed. The appendix was mesocecal, not inflamed or enlarged, but slightly adherent to the wall of the uterus, and because of this close proximity to the uterus, it was not removed. The abdomen was closed without drainage. The postoperative course was entirely uneventful, and the incision healed by first intention.

Uterine contractions began Dec. 3, 1935, nine days after operation, and after a labor of twenty-four hours which was complicated by cervical dystocia and maternal and fetal distress, the patient was delivered by internal podalic version and breech extraction following episiotomy and Dührssen's incisions in the cervix. The child was a normal, full-term, living female weighing 6 pounds 9 ounces (3,150 gm.). The puerperium was entirely normal, and the patient and her baby were discharged from the hospital in good condition on Dec. 15, 1935.

Pathologic examination of the right tube was made by Dr. C. G. Warner of the Department of Pathology who reported the following: The gross specimen was the distal 8 cm. of the right tube including a cystic mass 7 by 6 by 6 cm. It was a deep reddish purple color with prominent small vessels under the serosa. The peritoneal surface was smooth and glistening with no apparent inflammatory reaction.

There was a small cyst 1.0 cm. in diameter, close to the fimbriated extremity. On longitudinal section, the dilated tube contained a serous bloody fluid with some clots. The lining was somewhat trabeculated and was roughened by deposits of blood and pigment. The wall was 1.0 mm. thick about most of the periphery. The vessels on section were thrombotic. Microscopic examination showed hemorrhage into the wall of the tube and in the folds of the mucosa. Careful search revealed no evidence of tubal pregnancy.

NOTE.—Mrs. H. M. was readmitted to the University Hospital Nov. 18, 1936. The patient had been well since her discharge from the hospital in December, 1935. The last menstrual period was Feb. 19, 1936, and the estimated date of confinement Nov. 26, 1936. Her prenatal course was uneventful and was under the supervision of Dr. B. P. Warren. Labor began on Nov. 17, 1936, and after eleven hours the cervix was completely dilated. On Nov. 18, 1936 the patient was delivered of a full-term, living male child, weighing seven pounds thirteen ounces, L.O.A., by means of low forceps following an episiotomy. The third stage was uneventful. Inspection of the cervix revealed a laceration in the midline posteriorly about 6 cm. in length; this was immediately repaired. The total duration of labor was eleven and one-half hours. The immediate puerperium was entirely uneventful.

SUMMARY

1. Thirteen cases of twisted hematosalpinx complicating pregnancy are summarized from the literature; and a new case is added.
2. The condition occurs in young women; the youngest and oldest in this series were sixteen and thirty-six years, respectively.
3. Nine cases occurred before the seventh month of pregnancy.
4. The commonest symptoms were lower abdominal pain on the side involved, and nausea either alone or accompanied by vomiting.
5. The preoperative diagnosis was erroneous in each case. The commonest preoperative diagnoses were acute appendicitis and twisted ovarian cyst, in the order named.
6. In 12 out of the 14 total cases the right tube was involved, or in 85.7 per cent.
7. The size of the tumors in this series varied from that of a "hen's egg" to that of a mass filling the transverse width of the lower abdomen.
8. In 11 cases the pregnancy was not influenced and went to term. In Pinard's¹² case the patient was operated upon six hours after delivery; cesarean section was performed at the same time in the case reported by Stevens,¹⁰ and Taubenhau²⁰ resorted to the therapeutic abortion in his case, thirteen days after removal of the tube, because of the exhaustion of the patient.

I am deeply indebted to Dr. B. P. Warren, who sent the patient whose case history is reported to the hospital, for his kind permission to report this case; to Dr. C. R. Edwards who performed the salpingectomy; to Drs. L. H. Douglass and N. J. Eastman for their review of the material; and to Messrs. M. J. Schmulovitz and J. M. Cociomano for their assistance in the translation of some of the references.

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COMPARATIVE STUDY OF PELVIC TEMPERATURES UNDER VARIOUS THERAPEUTIC PROCEDURES*

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FOR the past several years much has been written about the use of heat as a therapeutic measure in pelvic infections. On our service at Lincoln Hospital we have employed the three types most commonly used, diathermy, Elliot treatment, and for the past year, the short wave radiotherm. This latter machine has a nine-meter wave length with an output of 200 watts. We became interested in knowing just what heat penetration was obtained with the three different methods.

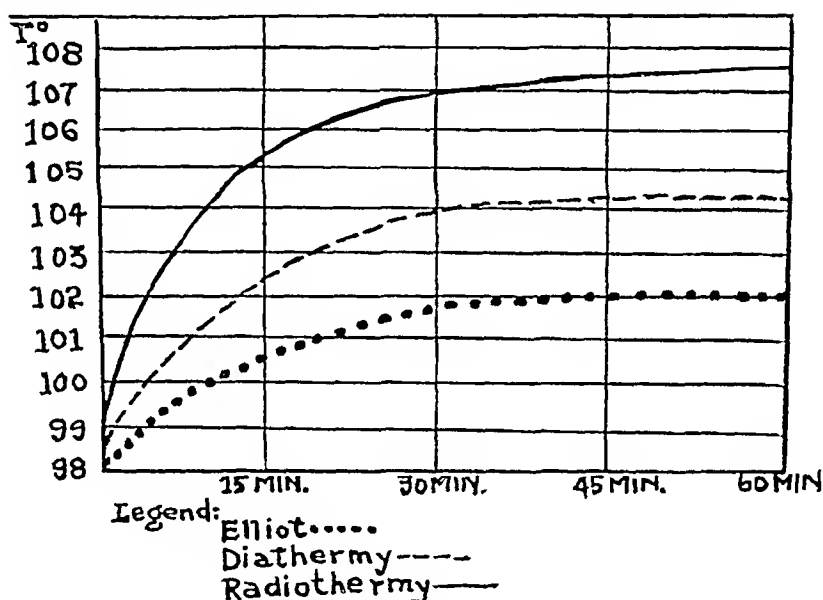


Fig. 1.—Intrauterine temperatures obtained under various therapeutic procedures.

The following procedure was carried out: The patients used were those who prior to the trial had dilatations and enrettages done for incomplete abortions. A silk bougie was passed through the cervix to the fundus of the uterus. In the diathermy and radiotherm treatments a vaginal applicator was then applied and the other electrode was placed on the abdomen just above the symphysis. In the Elliot treatment, after introducing the silk bougie into the uterus, the vaginal applicator was inserted. These treatments were all given for an hour. Temperature readings were taken at different intervals by means of introducing a thermocouple through the inserted silk bougie. No patient was given more than one treatment daily, although several of the patients were used for all three methods of treatment.

*Presented before the New York Obstetrical Society, May 12, 1936.

In our eighteen cases studied, several interesting facts were found.

First, that the size and obesity of the patient apparently has no bearing upon the intrauterine temperature obtained.

Second, that the highest cervical temperature which the patient will tolerate comfortably is 110° F.

Third, that this cervical temperature was obtained with the radiotherm in approximately five minutes; with the diatherm in about ten minutes, and with the Elliot treatment, which never reached above 109° cervical temperature, in about one-half hour.

Fig. 1 shows the intrauterine temperatures obtained. It was interesting to note that all of these temperatures reached the normal level in about five minutes after the treatment was discontinued.

DISCUSSION

DR. PAUL L. WERMER.—Dr. Ingraham neglected to remark that we reached temperatures of 107° F. at the fundus of the uterus by means of the radiothermy device. This evidently meant that heat was being effectively transmitted to the fundus and probably to the tubes. The temperature attained was thus close to the thermal death point of the gonococcus.

The machine we used was a nine-meter affair with compensator, computed to have a 200 watt output and 400 to 500 input. The thermocouple was of constantine and copper and sheathed in a No. 8 English catheter. The voltage generated was measured by a sensitive millivoltmeter capable of accurate readings at 1/100 of a millivolt.

DR. FRANCIS W. SOVAK.—With the use of the Elliot machine I had the opportunity to take some temperature readings during a laparotomy and at that time found the temperature of the culdesac 6° higher than normal and the temperature about the liver 1° higher than normal. The different temperatures in the peritoneal cavity were ascertained after the Elliot bag was in the vagina forty minutes.

DR. HENRY D. FURNISS.—The reason Dr. Sovak got his 6° rise was because he probably had the culdesac and the uterus isolated from the rest of the peritoneal contents, thus preventing dissipation of heat. Is that correct?

DR. SOVAK.—We simply made a small incision and inserted the thermometer before making the incision to get into the peritoneal cavity.

DR. FURNISS.—Herrick of Los Angeles did some experimental work along this line. He claims that with the Elliot apparatus and the bag in the vagina one never gets a temperature of over 102° in the uterus or the urethra. With very low frequency and ordinary diathermy you get the greatest degree of heat at the region of the greatest electrical resistance. If you place one electrode on the skin of the abdomen and one over the back the current does not necessarily go straight through from the one to the other; it may go around. To get the heat effect, one of the electrodes must be in one of the orifices, such as the urethra, the cervix, or the vagina.

DR. INGRAHAM (closing).—I think the temperature that Dr. Sovak obtained in the culdesac is easily accounted for, as the culdesac is practically in apposition to the vaginal applicator of the Elliot machine. Thus it is practically the cervical temperature which we give as 109°.

TUBOOVARIAN PREGNANCY

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THIS case is the only tuboovarian pregnancy thus far observed at the Woman's Hospital.

Halban-Seitz Handbuch,¹ discussing tuboovarian pregnancy, prefers to call it "ovary-tube" pregnancy and states that such is only possible if both the tube and ovary take part in the formation at the site of the implantation. He believes there must have been a preexisting fusion of the tube and ovary before impregnation. Furthermore, the fimbriated end of the tube may spread out over the ovary and become sealed to it, or the fimbriated end of the tube may close off entirely and the ovary become fused to the tube at an accessory lumen. No matter which method of sealing the tube to the ovary takes place, the follicle can ripen immediately below the lumen (in one case the fimbria and in the other the accessory) and the ovum in either case has access to the cavity of the follicle. After fertilization occurs, implantation may occur either on the tubal portion of the "ovary-tube" lumen or canal, or on the ovarian portion, and the distinction can be made as either primary tubal or primary ovarian "ovary-tube" pregnancy. Schumann,² in an excellent treatise on extrauterine pregnancy, states that one deals with a tuboovarian pregnancy when the fetal sac is composed partly of tubal and partly of ovarian tissue. The fimbriated end of the tube has previously to be adherent to the ovary.

The patient, white, American, twenty-three years of age, began to menstruate at eleven years of age, every twenty-eight days for four days. No pain or clots. Last period Oct. 23, 1933. Married three years. One full-term pregnancy one year ago, normal delivery and puerperium. Pneumonia at sixteen years. Entered the Out-Patient Department on Jan. 18, 1934, where a diagnosis of probable ectopic pregnancy was made and she was immediately admitted. Her chief complaint was that twenty days after she began to menstruate she had vaginal spotting for sixty-seven days. She complained of occasional mild cramplike pains in the left lower quadrant. A month before she had a fainting spell. Examination revealed a normal well-developed woman. The pelvic floor was slightly lacerated but had good function. The cervix was one and a half times normal size. The uterus, anterior and to the right, was twice normal size, with a possible myoma. A diagnosis of intrauterine pregnancy was made, since practically no tenderness was elicited on examination. An ectopic was scarcely suspected. Urine negative. Blood, R.B.C. 3,900,000; Hg 85; W.B.C. 11,200; polymorphonuclears 72; lymphocytes 28. Wassermann negative. Sedimentation time: first hour 22 mm. (82 min.). An Aschheim-Zondek test was positive. A consultant stated: "pregnancy (ectopic?), mass behind the uterus and to the left side. Diagnosis, threatened abortion? Watch and wait. Examine frequently." On the eighth day after admission, not because of any pain or any fainting, but because the staining still persisted and the mass on the left side seemed to be increasing, the patient was operated upon.

Operation.—Cervix soft and firmly closed. Uterus had a measured depth of 11 cm., was pushed over to the right and contained a large amount of decidual tissue. There was a boggy cystic mass about 10 cm. in diameter in the left adnexal area, part of which was ovary and part tube. This was apparently an ectopic which had ruptured through the fimbriated portion of the tube, not unlikely into one of the ovarian cysts,

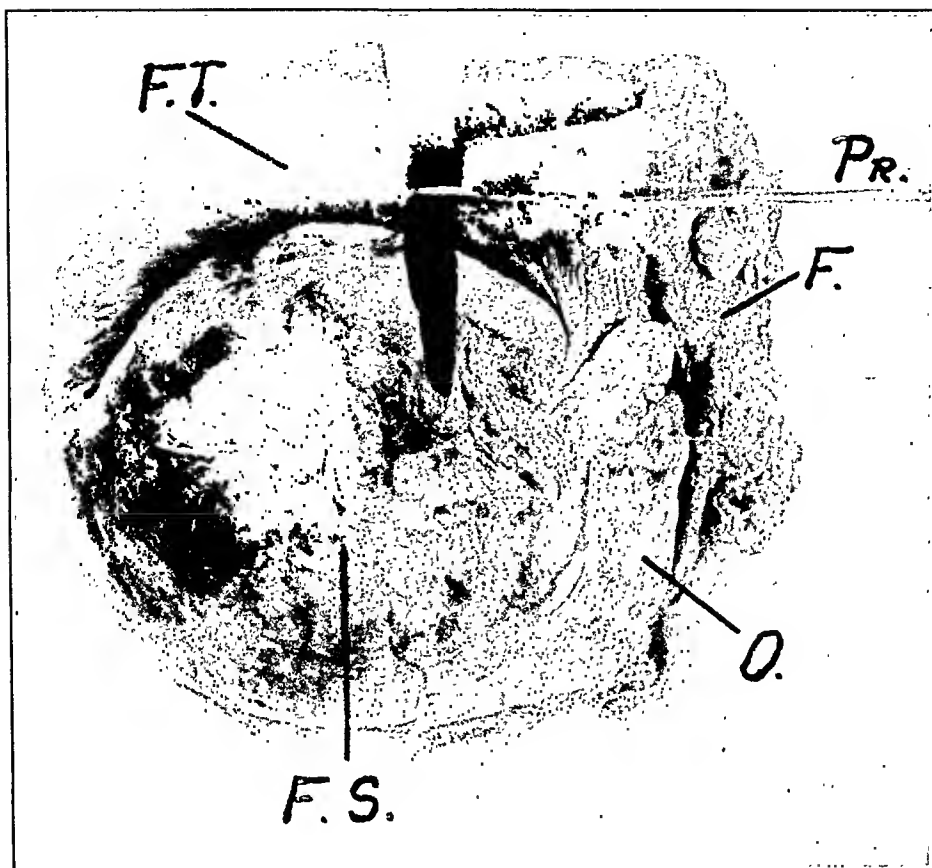


Fig. 1.—*F.T.*, Fallopian tube. *Pr.*, Probe in ostium fallopian tube. *F.*, Fimbriae fallopian tube. *O.*, Ovary. *F.S.*, Fetal sac.

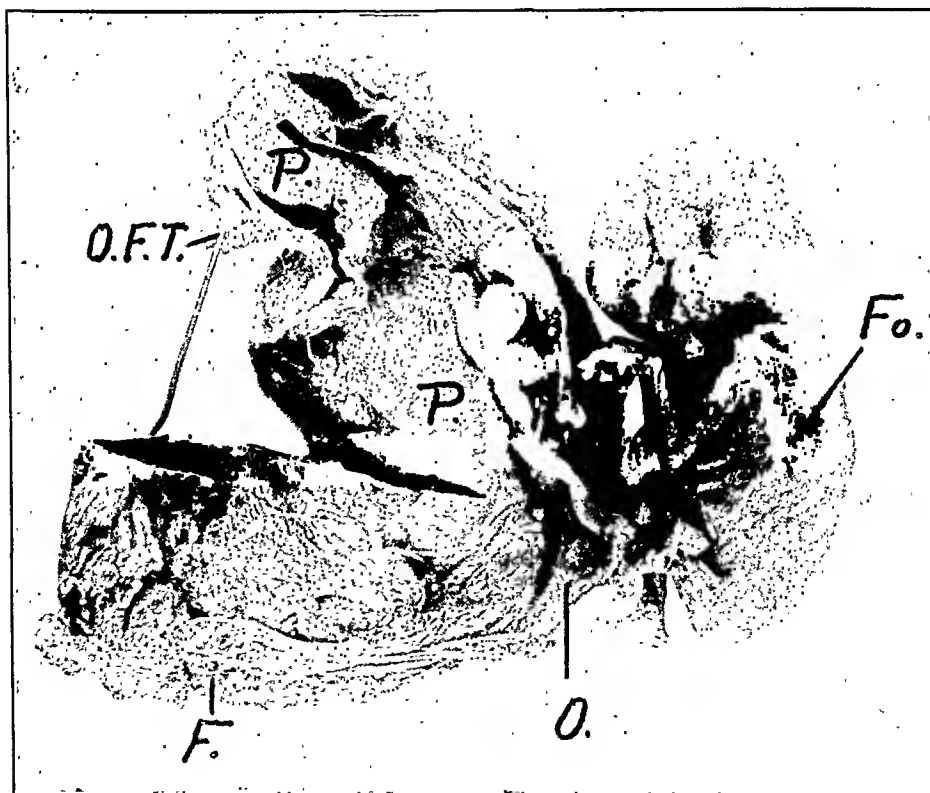


Fig. 2.—*P.*, Placenta. *F.*, Fimbriated fallopian tube. *Fo.*, Fetus. *O.*, Ovary. *O.F.T.*, Ostium fallopian tube.

but it could not be definitely made out where the ectopic insertion was. There were about 300 c.c. of clotted blood in the culdesac, and from 150 to 200 c.c. of fluid blood free in the abdominal cavity. There were no adhesions except that the whole mass was adherent to the posterior wall of the uterus and to the culdesac by light adhesions, probably organizing blood clot.

Frozen section revealed decidua but no malignancy, and no evidence of chorionic elements. The abdomen was then opened by a low transverse incision and left

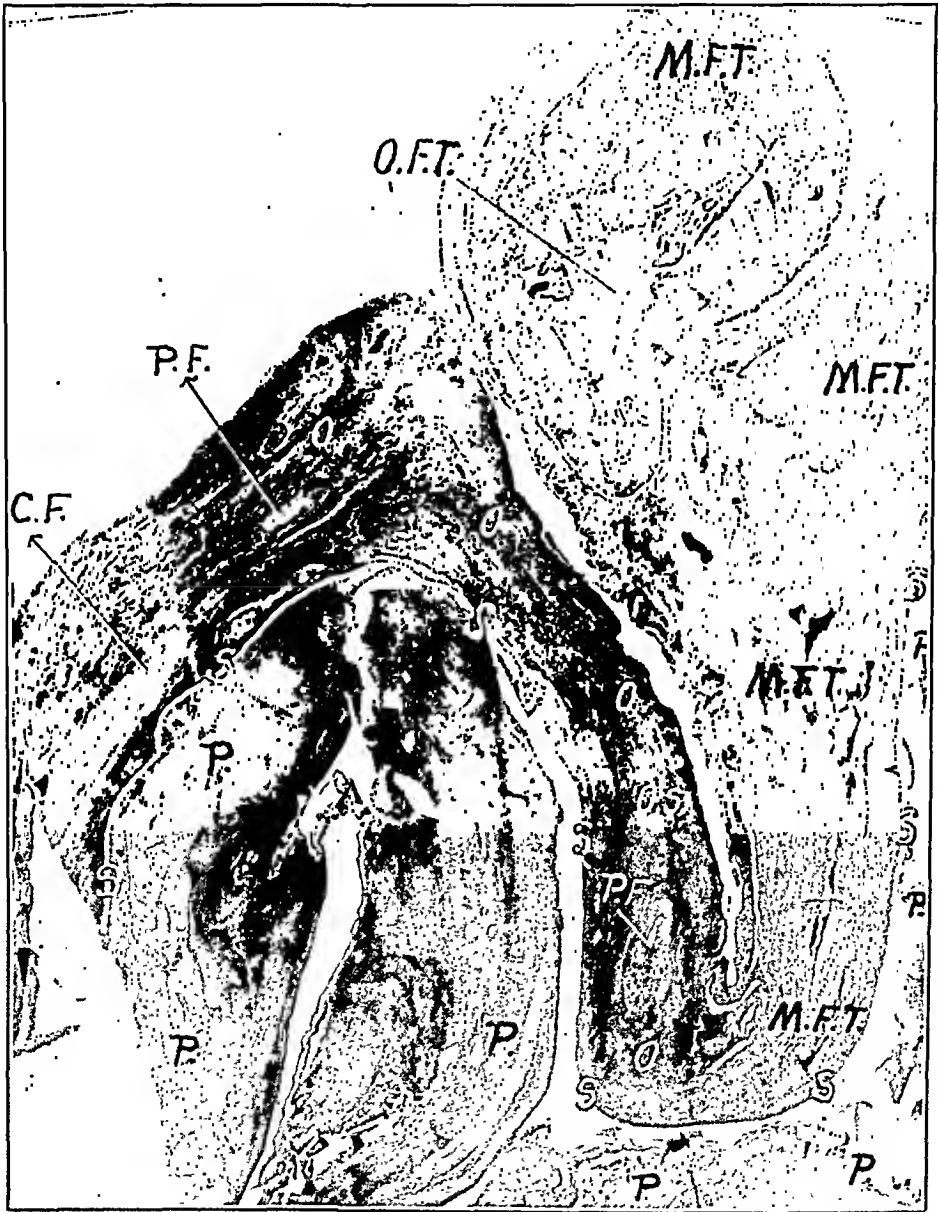


Fig. 3.—*P.*, Placenta. *O.*, Ovary. *S.*, Placental attachment. *O.F.T.*, Ostium fallopian tube. *M.F.T.*, Muscle fallopian tube. *O.S.*, Ovarian stroma. *C.F.*, Corpus fibrosum. *P.F.*, Primordial follicle.

salpingo-oophorectomy done. Anesthesia: Nitrous oxide, oxygen and ether. Pre-operative blood pressure 100/40. Postoperative blood pressure 96/55. Time of operation: one hour 2 minutes. On the same day the patient was given a transfusion of 450 c.c. of blood by the Scannell method. She had a normal convalescence, her incision having healed by primary union, and she left the hospital on the eighteenth day in good condition.

Pathologic Findings.—The curettings were composed of well-developed decidua without any evidence of degeneration. Chorionic elements were not detected. The abdominal specimen (Figs. 1 and 2) (macroscopic) consisted of a pregnancy sac 9 by 6 cm. in diameter, to which was attached an isthmic portion of the tube 5 cm. long, extending from the upper margin of the cystically distended ampulla to the abdominal parietes. The tube wall was missing at about half of the surface and the edges of the preserved tube wall revealed previous rupture. Old blood was accumulated between the contents of the cystic portion and the tube wall. Fresh blood was clinging to the outer surface. The fetal sac was intact, except for some fragmented chorion which hung loosely from the opening. The amniotic fluid was clear. The embryo, a normal male, measured 12.5 cm. The umbilical cord was tortuous, formed two large varicosities 1 cm. from the embryo. The ovary could be separated from the tube wall only in its upper margin, while its lower part was fully incorporated in the tube wall. Its approximate size following outlines was 5.5 by 4.0 cm.

Incision through the sac: A cut exposing the wall of the fetal sac revealed it furnished both by the tube and by the ovary, the one transgressing into the other without obvious limit. Thus, only the proximal third of the tube was preserved while the distal portion was completely used up in the formation of the fetal sac. *Microscopic* (Fig. 3): A section through the deep notch in the wall of the fetal sac revealed it composed on one side by atrophic or stroma including compressed atrophic graafian follicles and corpora fibrosa, and on the other side by stretched atrophic tube wall with small remains of the mucosa. The fetal sac was incompletely intercepted by the described fold formed by ovarian tissue and tube wall at the side of their junction, simulating two fetal cavities. In both partitions, the fetal layers were well preserved except for both areas where hemorrhage had occurred between the area of nidation and the chorionic structures. The chorionic tissue showed extensive fibrosis of the stroma of villi. Sections of other parts of the cystic cavity revealed similar pictures. *Diagnosis:* Tuboovarian pregnancy, twelve weeks of age, unruptured. Intrauterine decidua.

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Ordinarily a delay in menstruation of two or three weeks in women who are habitually regular is considered as due to an early abortion. However, in the presence of our new knowledge concerning hormones such a diagnosis should be made with caution. The authors report a series of cases where menstruation was delayed and they believe the delays were due to a disturbance in the rhythmic and successive action of follicular and luteal hormones on the uterine mucosa. Such disharmony may produce a decidual reaction in the absence of a fertilized ovum. In the authors' cases they could not prove their contentions but as probable evidence they cite the fact that the biologic reactions of the urine were negative and the delay in menstruation was seen in some women whose husbands have azoospermia. In cases of pseudo-pregnancy and sterility it is important to rule out ectopic pregnancies. This can readily be done by means of urine tests. Ordinarily it is believed that a hypersecretion of progestin delays menstruation, but the authors believe that follicular cysts may produce the same results by bringing about a temporary polyhormonal amenorrhea.

J. P. GREENHILL.

FATAL AIR EMBOLISM ON THE EIGHTH DAY OF THE PUERPERIUM

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FATAL embolism resulting from the entrance of air into the veins of the uterus has been described many times as a result of attempts at criminal abortion, less frequently as a complication of labor at full term and in these cases usually immediately postpartum. In many, some condition was present necessitating interference such as placenta previa or postpartum hemorrhage.

Gough¹ reported air embolism in a woman of twenty-five in her second labor. Forceps delivery had been done for prolapsed cord when the anesthetist reported that the patient had collapsed. The pulse, unobtainable at the wrist, was 170 obtained from the abdominal aorta, dyspnea was marked, the patient in extreme pallor, cyanosis developing just before death. The patient regained consciousness for a time, then coma supervened. Restlessness was extreme, requiring restraint, death occurred seven hours after delivery.

Autopsy showed the right ventricle markedly dilated, with flabby walls which appeared transparent. Opened under water the right ventricle was found to contain much free air and a little frothy blood. The pulmonary arteries also contained frothy blood; there were no thrombi.

One other case was found in the literature of a fatal air embolism as late as the eighth day postpartum after a normal labor and puerperium. This case was reported by May in the *British Medical Journal*, June 6, 1857.

Symptoms described in the collected cases were: A sense of oppression about the chest, a feeling of sinking or exhaustion, extreme restlessness, dyspnea and faintness, convulsive movements were noted in two. Pallor was noted in many cases and in a few cyanosis was a terminal symptom. Death was immediate in 17 cases, after "several hours" in two cases, after five hours in one case, less than one hour in one case, "after a short time," one case.

Three died in physicians' offices after attempts to produce abortions.

It is evident from the literature that the occurrence of death from air embolism as a complication of an otherwise normal pregnancy, labor, and puerperium and occurring as late as the eighth day postpartum is very rare and merits an additional case report.

L. M. H., hospital number 89052. This twenty-six-year-old housewife, a gravida iv, was first seen in the Rochester General Hospital prenatal clinic, Sept. 1, 1935. Her last menstrual period was May 11, 1935, and was normal in character. Up until the time she was seen her pregnancy was uneventful. Her family history was essentially negative. Her father died of typhoid fever. Her mother and one sister were living and well. The patient had typhoid fever at three years of age, measles and whooping cough in childhood. She had frequent attacks of tonsillitis as a child. Tonsillectomy at six years of age. No illness since that time. Her periods were regular, with some pain the first two days. Moderate flow.

She has had 3 previous pregnancies, 2 of which were uneventful and terminated in spontaneous deliveries of normal living children. Had normal puerperiums after both deliveries, the last one in January, 1933. The third pregnancy terminated at home in a spontaneous abortion at three months.

On October 22, 1935, she was admitted to the obstetric service because of premature rupture of membranes (sixth month of pregnancy). She complained of some low backache which she had had for about five weeks. She presented no toxic symptoms. Blood pressure was 110/68. No edema.

The fetus was active. Vaginal examination the day after admission showed that the head was not engaged and that the cervix was closed and not effaced.

She had no vaginal drainage after admission to the hospital. She had an attempted medical induction of labor with castor oil and quinine which was not successful and she was discharged three days after admission to be followed in the prenatal clinic. She continued to have some watery vaginal discharge at intervals and some backache but no other complaints. On Jan. 1, 1936, she was again admitted to the obstetric service because of the onset of pains which were mild and recurred every fifteen minutes. She had no vaginal drainage or discharge at this time.

Examination at this time revealed nothing of note. Her blood pressure was 110/86. Urine was negative. Rectal examination showed that the head was not engaged but that the cervix was patulous but not effaced. Pains ceased soon after admission and she was again given castor oil and quinine but did not go into active labor and was discharged on the third day to the prenatal clinic.

She was seen each week and on Jan. 23 she had again lost considerable fluid and had been having some bloody show for three days. She was again admitted and labor was induced. She went into labor and delivered spontaneously, after an eight-hour labor, of a 6 pound, 12 ounce normal female child (vertex R.O.A.). Very little postpartum bleeding.

Following delivery she ran a perfectly normal postpartum course. Her temperature was never above 98.6° F. Lochia was normal and at no time abnormally profuse. Her breasts began secreting on the fourth day. On the seventh postpartum day she was in knee-chest position thirty minutes in the morning and afternoon. On the morning of her eighth postpartum day she was again put in knee-chest position. She had been up in the position five minutes when, without any outcry or warning, she fell out of bed. When the nurse, who was in the ward at the time, reached her she was pulseless, gasping for breath, and had an ashen, cyanotic color. She was seen by a house officer about five minutes later but by this time her respirations had ceased and heart sounds could not be obtained. A clinical diagnosis of massive pulmonary embolism was made. Autopsy was obtained and done four hours after death.

Report of Autopsy Findings.—The body was that of a well-developed, well-nourished white female, twenty-six years of age. Breasts well developed and contained milk. Abdomen was that of a postpartum patient. Uterus could be felt just below the symphysis pubis. No edema or scars of lower extremities.

Chest: There was a small amount of clear pericardial fluid. The heart was in normal position. The right ventricle was much distended, it was ballooned up and on palpation felt like being full of air. The pulmonary artery was distended and seemed to contain air. When the pericardial sac was filled with water in situ and the right ventricle opened, a large amount of air escaped and also a small amount of frothy red foam. The right auricle, ventricle, and pulmonary artery contained no postmortem blood clots, no blood clot emboli, only very little frothy blood. The left ventricle and aorta contained no air. Myocardium, endocardium, and valves were normal. Coronary arteries were patent. The aorta was normal. *Lungs* showed some acute emphysema, otherwise normal. *Abdomen:* Liver, gallbladder, spleen, kidneys, adrenals, and pancreas were of normal size and position, and they showed nothing abnormal. Stomach and intestines were also normal. The *right ovarian plexus* was much distended and filled with a great many air bubbles. The left ovarian plexus, however, did not seem to contain air. Uterus measured 12 by 16 by 8 cm. and was about the size of a newborn's head, definitely subinvolved. Section revealed hypertrophied, but otherwise normal muscle tissue without the slightest evi-

dence of crepitation. The uterine cavity appeared to be moderately distended and contained about 60 to 80 c.c. of dark red liquid blood. Attached to the posterior wall and adherent to it was another brownish red blood clot, 10 by 5 by 2 cm. in size, apparently with beginning organization. This old blood clot was covered by several fresh dark red blood clots which were very easily removable. At the lower pole of

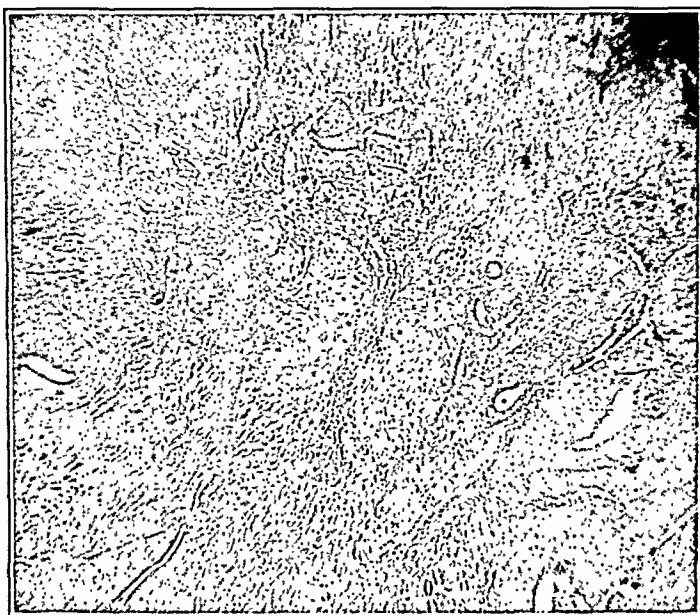


Fig. 1.—Retained small pieces of decidua tissue surrounded by blood clot.



Fig. 2.—Same as Fig. 1, but with higher magnification.

the old clot was another fresh clot which was lying free in the cavity (Fig. 1). The lower pole of the old blood clot was separated from the uterine wall. Upon raising this part of the old clot, three freely gaping, patulous sinuses, about 3 or 4 mm. in diameter, could be seen. There were clots in the other sinuses in that region. The rest of the uterine surface was smooth and showed no signs of infection.

Ovaries, tubes, bladder, and rectum showed no remarkable pathology. *Histology:* Several blocks were cut at different levels from the uterus in the region of the adherent blood clot. In these sections *retained decidua tissue* with some chorionic villi was found surrounded by blood clots and hemorrhages (Fig. 2). In the uterine wall just beneath this area there were much distended uterine veins filled with thrombi and some of these showed early organization. Blocks were also examined from other parts of the uterus. In these regions there was no evidence of endometritis, there was no necrosis of the muscle and there were no gas bubbles in the wall.

Anatomic Findings.—(1) Moderately subinvolved uterus eight days postpartum. (2) Retained small pieces of placental tissue with surrounding hemorrhages and blood clots. (3) Sudden death due to air embolism at the time of changing knee-chest position. Air was sucked in probably through the opened large uterine veins. (4) Dilatation of heart, right ventricle, due to the presence of much air. (5) Marked distention of right ovarian plexus due to abundant air bubbles.

Cause of Death.—(1) Fatal air embolism by way of opened uterine sinuses. (2) Retained small pieces of decidua tissue with hemorrhage.

In this case it is easy to reconstruct the mechanism of this accident. There evidently had been some bleeding from the placental site due to the retained small particles of decidua tissue. Blood clots were formed not only around the retained small pieces of decidua tissue but also in numerous uterine veins just beneath this area. As the patient went into the knee-chest posture, the lower pole of this blood clot became separated from the uterine wall and several large veins became opened. At first hemorrhage occurred which was suddenly followed by the suction of air into these gaping veins in sufficient quantity to block the pulmonary artery and the right side of the heart.

The case is that of a real air embolism, in which the origin of the embolism from gas bubbles, produced by bacterial agents, was sufficiently ruled out.

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Gardner, Smith, Allen, Edgar, and Strong: Cancer of the Mammary Glands Induced in Male Mice Receiving Estrogenic Hormone, Arch. Path. 21: 265, 1936.

Mammary cancer develops spontaneously in female mice of certain strains; it seldom or never occurs in males. Feminization of the male mouse by ovarian grafts induces a partial growth of the mammary glands. Mammary cancer can be induced in male mice receiving estrogenic hormone over an extended period. The development of mammary cancer appears to be a sex-limited character in the mouse. The following experiment was made: Two of six male mice from one litter of the A strain were subjected to weekly injections of 500 international units of keto-estrin benzoate in oil. Two carcinomas developed in one mouse and one in a second mouse. The female mice of this strain are susceptible to spontaneous mammary cancer. The pattern of mammary growth induced in these animals was abnormal in that the growth of the duct system was restricted or stunted and the mammary lobules developed extensively. This work has been verified further by additional animals showing the same results. These tumors appeared in mice at ages varying from 162 to 362 days and after the mice had received from 10,000 to 18,000 international units of keto-estrin benzoates. Four of the mice were under 200 days of age at the time that the tumors were observed.

W. B. SERBIN.

A FULL-TERM PREGNANCY COMPLICATED BY AN ACUTE INTESTINAL OBSTRUCTION AND FALSE LABOR PAINS*

JOHN CASAGRANDE, M.D., BROOKLYN, N. Y.

ACUTE intestinal obstruction complicating pregnancy is relatively rare. Bemis¹ states that only 13 cases were reported in the American and British literature from 1900 to the time of his report in 1931. Since this time I have found only four other reported cases, including his, one each by Cornell² and Blair,³ and one by Kornfeld and Daichman.⁴

At the Brooklyn Hospital we have had two cases of acute intestinal obstruction complicating pregnancy in 11,246 cases, covering a period of ten years.

The present case is reported because it presented an interesting problem in diagnosis as well as a difficult decision on the time for surgical intervention in view of the uncertain status of labor.

The patient was a twenty-nine-year-old para ii. Her prenatal record showed nothing of interest. Her previous history included a laparotomy in 1926 in Norfolk, Virginia, performed for chronic appendicitis, a cystic right ovary, and a retroversion of the uterus. The appendix and right ovary were removed and a Crossen's suspension of the uterus was done, the round ligaments being shortened by sewing them to the posterolateral surface of the uterus, thus correcting the retroversion and at the same time utilizing them to peritonealize the raw surfaces. One week after discharge she was readmitted for an incision and drainage of an ischiorectal abscess. In 1929 she had an uncomplicated delivery of a full-term fetus at the Brooklyn Hospital.

The patient's present history began two days before admission, at which time she appeared in the emergency ward of the Brooklyn Hospital, complaining of lower abdominal pain. The examining interne made a diagnosis of impending labor complicated by a degenerative fibroma. She refused admission and signed a release form, and several hours later the pain subsided spontaneously. Two days afterward, however, at 3:15 P.M. on October 15, 1935, she was admitted to the obstetric service, complaining of intermittent cramplike pains in the lower abdomen occurring at intervals of ten to fifteen minutes, which began at 12:15 P.M. the same day.

It was assumed that she was in labor. Her last period had occurred Dec. 28, 1934, making her theoretically overdue eleven days. Four hours after admission, it was reported that the patient was having severe bearing-down pains and, as no presenting part could be felt in the brim, a malpresentation or position was suspected.

Examination at this time showed an uncooperative highly nervous patient, complaining of irregular intermittent pains in the lower abdomen. Her general condition was good. Her temperature was 97°, pulse rate 80, and blood pressure 110/70. The urine showed a faint trace of albumin, with a two-plus acetone and a few hyaline and granular casts. She had vomited a small amount of bile soon after admission and had had two spontaneous bowel movements that morning.

The abdominal examination disclosed a full-term pregnancy. The fetal heart rate was 128, heard best in the right lower quadrant. Strong uterine contractions lasting forty seconds were recurring every four to five minutes. There was a soft, tender, compressible mass, dull on percussion, extending from the pubes and left groin to just below the umbilicus. Vaginal examination showed an unengaged vertex presenting, the cervix was open one finger but not effaced, and the membranes intact. It was at first thought that the mass might be a distended bladder, mis-

*Presented at a meeting of the Brooklyn Gynecological Society, March 6, 1936.

placed as a result of her previous pelvic operation, and so the patient was catheterized and four ounces of urine obtained, with no effect on the mass.

The patient at this time began to get drowsy and her pain disappeared, probably as a result of morphine given one hour previously. It was accordingly decided to reexamine her in two hours to determine whether the patient was having a false or true labor. The effect of the morphine soon wore away and the severe pains and strong uterine contractions returned, but since there was no further dilatation of the cervix, it was assumed that the patient was having a false labor and that sur-



Fig. 1.—Showing a portion of strangulated ileum passing through a rent in the left broad ligament just beneath the round ligament.

gery might be indicated for the tumefaction. A blood count at this time showed 95 per cent hemoglobin, 4,800,000 red blood cells. There were 19,900 leucocytes with 95 per cent polymorphonuclears, and 5 per cent small lymphocytes. Immediate operation was decided upon after further surgical and obstetric consultation, because of the uncertain status of labor.

The patient was then given $\frac{1}{4}$ gr. of morphine by hypodermic and a 1500 c.c. clysis, preparatory to laparotomy. At the operation it was found that six to eight inches of what appeared to be devitalized ileum had passed through a rent in the peritoneum just beneath the previous operative attachment of the left round

ligament. The rent in the broad ligament was obliterated by suturing. The devitalized ileum was brought through a stab wound preparatory to an ileostomy which was done thirty hours later. Following the laparotomy she was given generous doses of pantopon with the hope that labor would be delayed at least twenty-four or forty-eight hours. Her immediate postoperative reaction was satisfactory.

The onset of labor occurred at 1 P.M., October 17, 1935, thirty-six hours after operation. A Beck binder was applied, pantopon given for analgesia, and the patient was told not to bear down. Three hours later she was fully dilated, the membranes were ruptured artificially, and the vertex engaged in the brim in an R. O. P. position. Under gas oxygen and ether anesthesia an unsuccessful attempt to rotate the head anteriorly with the Kielland forceps was made. The Dewees' forceps were then applied, and after considerable traction the vertex was brought down to the pelvic floor and a Scanzoni maneuver was done just as the vertex reached the perineum, thus converting an R. O. P. into an R. O. A. The Elliot forceps were then used to complete the delivery of a normal baby, weighing 8½ pounds. No lacerations resulted. Her postpartum convalescence was uneventful. The mother and baby were discharged sixty-one days after admission.

COMMENT

The error in assuming that this patient was in labor on admission is readily understandable since she was at term, in fact theoretically past due, and she had definite uterine contractions which increased in frequency and duration.

In reading over reports which closely parallel this case, I have noted that uterine contractions simulating labor pains were common enough frequently to mask the true diagnosis. I venture to say that labor would have begun sooner in this case had the obstruction not been relieved. Just why uterine contractions simulating labor pains in this case and others paralleling it, occur, is apparently not known. In this patient it was probably direct irritation caused by the strangulated gut, part of which was in direct contact with the anterior surface of the uterus.

The report of the interne was incorrect when he thought that there was a malposition or presentation because the presenting part was not entering the pelvis, even though the patient was apparently having very hard bearing down pains. But this observation was important, as it led to a more intensive survey and surgical consultation, with the much needed operative intervention.

After the decision to operate was made, two problems were discussed. The first was whether the patient was actually in labor, and, if so, would she deliver in a matter of a few hours? The surgeon would have risked delaying the operation a short time, if we could have assured him of a relatively quick vaginal delivery. Since we could not do this, the other problem arose, namely, should pregnancy be terminated by cesarean section and followed by whatever other surgery was indicated, or should the necessary surgery be done and the pregnancy allowed to terminate via the natural passages? In general the principle of treating complications and allowing nature to take care of the pregnancy seems wise, and I believe this principle is generally accepted.

The exception to this would be in the very rare cases where an obstruction of the sigmoid is caused by direct pressure of the gravid uterus or the presenting part as it crosses the pelvic brim, as in the case reported by Blair. It is obvious that a cesarean section would then be a proper expedient to relieve the obstruction.

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TWO CASES OF UNRUPTURED ECTOPIC PREGNANCY*

MILTON M. SCHEFFLER, M.D., CHICAGO, ILL.

(From the Department of Surgical Pathology of the Cook County Hospital)

THESE two cases of unruptured ectopic pregnancy are being presented because of the diagnostic difficulties encountered, the large size of the specimens, and their association with salpingitis.

CASE 1.—Colored female, aged thirty-nine years, gravida i, para 0, had a spontaneous abortion three years prior to admission to the hospital, and now entered complaining of pain in the right lower quadrant for eighteen days. The onset had been ushered in with vague abdominal distress, followed after four days by severe sticking, knifelike pains in the right lower quadrant, lasting for a few hours and then replaced by a generalized cramping pain, the latter lasting for a few days. The pain again localized to the right lower quadrant where it remained up to her admittance to the hospital. A venereal history was denied, but the patient stated that a discharge had been present since her marriage.

Her menstrual periods had been regular up to December, 1935, when they became irregular and more frequent. That month she had two periods, the first coming at its regular time, lasting three days with a moderate flow, and the second fifteen days later, lasting only one and one-half days with a scanty flow. In January she again had two periods, at approximately the same time, the first period lasting five days with the flow quite profuse for the first three days, the second lasting again five days but the flow quite scanty. Dysmenorrhea was not present at any time.

Physical examination revealed a well-nourished, well-developed colored female who did not appear acutely ill. Temperature was 99.8°, pulse 88, respirations 20, and blood pressure 116/82. The abdomen was somewhat distended with moderate rigidity over the lower quadrants and tenderness in the lower abdomen, more marked in the right lower quadrant. Pelvic examination revealed a moderate, foul discharge. The tip of the cervix was somewhat softened. An elongated irregular mass was felt in the right adnexal region extending from the uterus and quite tender. Laboratory findings were essentially negative. The impression at that time was a chronic salpingitis with tuboovarian abscess, though an incomplete tubal abortion had to be considered.

At operation the uterus was found softened and fixed by adhesions in the pelvis and the middle two-thirds of the right fallopian tube was converted into a mass 6 by 5 by 4 cm., soft and purplish red. The fimbriated ends of both tubes were occluded and the left tube was thickened. On sectioning this mass, a cavity 3 cm. in diameter was exposed and was found to be filled with a yellowish fluid and adherent to the lining by a stalk was a 13 mm. fetus approximately five to six weeks old. The wall of the sac was 9 mm. thick and dark purple gray.

CASE 2.—A white female, aged thirty-six years, gravida iii, para iii, whose last child was born in 1933, entered the hospital because of abdominal pain of five weeks' duration and vaginal bleeding. Language difficulty resulted in a rather meager history. Indefinite abdominal pain had been present for the past five weeks, being dull, aching in character with occasional sharp pain in the left lower quadrant. A venereal history was denied. Her menstrual periods had always been regular until December, 1935, when she missed a period. In January she menstruated scantily for two days. On the morning of admission she had had slight vaginal bleeding.

*Presented at a meeting of the Chicago Gynecological Society, March 20, 1936.

Physical examination revealed a well-nourished, well-developed, white female of thirty-six years, who did not appear acutely ill. Temperature was 100°, pulse 88, respirations 18, and blood pressure 118/70. Pelvic examination revealed that the cervix was firm and closed, the uterus slightly enlarged and deviated to the right. A hard nodular mass was palpated in the left adnexal region and not attached to the uterus, but pushing it to the right. No tenderness was elicited. The laboratory findings revealed a normal blood count (white cells 9,800, red cells 4,000,000, and hemoglobin 80 per cent). X-ray of the abdomen showed a small amount of air underneath the right diaphragm. Wassermann test and urine were negative. The impression at this time was that of an ovarian cyst with functional bleeding. An ectopic pregnancy had to be ruled out and an exploratory operation was advised.

At operation the left fallopian tube at its isthmic portion was found converted into a mass 7 by 6 by 5 cm., deep purplish red and soft. The distal portion of the tube was fused with the ovary to form a mass 6 by 5 by 1 cm. and was markedly thickened. On section of the larger mass, the wall was found to be up to 2 cm. in thickness, and a cavity was exposed lined by a purple brown membrane and attached to this by a stalk was a 10 mm. fetus about four to five weeks old.

Of added interest in conjunction with the two cases just presented is an analysis of 50 cases of ectopic pregnancies encountered by the Surgical Pathology Department of Cook County Hospital in 1935. A correct diagnosis was made in 70 per cent of the cases, while in the unrecognized ones, the most common diagnosis was a chronic salpingitis. Appendicitis, ovarian cysts, and pelvic peritonitis followed in the order named. Of these 50 cases, 32 per cent were found to be ruptured at operation. Salpingitis, which is thought to be a common finding, especially in those patients seen at Cook County Hospital, was present in only 16 per cent of all the cases, the diagnosis being based on gross and microscopic findings at the site of gestation.

COOK COUNTY HOSPITAL

EMPHYSEMATOUS VAGINITIS

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FORT WORTH, TEXAS

EMPHYSEMATOUS vaginitis, or colpitis emphysematosa, is a rare condition that occasionally occurs during pregnancy. Ingraham and Hall recently reviewed the literature and reported three cases.*

We are presenting a case in which this unusual condition occurred twice within a period of two years. Both clinical and histologic studies were made, but no cultures or examinations of the gas content of the cysts were carried out.

Mrs. M. M. was first seen in April, 1932. She was then twenty-four years old and had been married three years, with no pregnancies. Her chief complaint was dysmenorrhea for the past twelve months. During the past four months she had noticed that immediately following each menstrual period she would have an irritating discharge, scant in amount. Concurrent with the discharge small white blisters would appear on the labia, accompanied by considerable itching and burning. The blisters would disappear in from one to three days to recur following the next menstrual period. There was no discharge or other discomfort between periods.

Examination, revealed innumerable small blebs or blisters, in the fornices of the vagina, with a greater number on the posterior wall. These were small distended

*Ingraham, Clarence B., and Hall, Ivan C.: *AM. J. OBST. & GYN.*, 28: 772, 1934.

cysts in the mucosa of the vaginal wall and cervix. The cysts were discrete, firm, and could not be displaced as in subcutaneous emphysema. They occurred in clusters, interspersed with normal-appearing vaginal mucosa. A fold of mucosa on the right posterolateral wall was studded with the gray, glistening cysts. Tissue was removed from this fold of mucosa for pathologic study. The pathologic report follows:

The biopsy specimen consisted of two slightly wedge-shaped cystic pieces of tissue. Both pieces floated partially submerged when placed in water. One surface of each

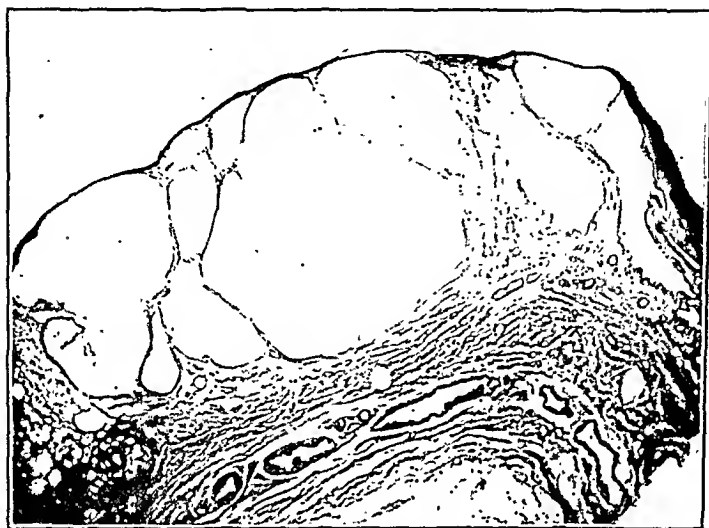


Fig. 1.—Section showing large spaces or vesicles just beneath the mucous membrane; mucous gland tubules in deeper layers of tissue.



Fig. 2.—Section showing vesicle wall of fibrous tissue without lining cells.

piece was covered with multiple small cysts or blisters that varied from pinpoint to 8 mm. in diameter. The small cysts lay just beneath the mucous membrane and when broken, made a slight noise. The vesicles were empty. The largest piece of tissue measured 2.5 by 2 by 1 cm. Histologic examination revealed loose fibrous connective tissue, one surface being covered with a thin layer of well-differentiated squamous epithelial cells. Just beneath the epithelium were multiple, small varying sized spaces that had no definite lining cells. The surrounding fibrous tissue was

edematous and in some areas diffusely infiltrated with lymphocytes and a few leucocytes. A number of thin-walled blood vessels were present but were not distended with blood.

The patient was instructed to use alkaline douches, and for several months following the removal of the biopsy there was no recurrence of the vesicles. The vaginal discharge continued, however, and on May 27, 1933, the cervix was cauterized; at that time no blisters were seen.

Early in 1934 the patient became pregnant and was under the care of one of us from February through May. On May 9, 1934, she had a spontaneous abortion following vaccination for smallpox. During this pregnancy there was no noticeable recurrence of the emphysematous cysts. In September, 1934, the patient was again pregnant, and at that time there was a recurrence of the emphysematous cysts. On October 15 and again on October 31 it was necessary to open as many of the large blisters as possible for relief of pressure of which the patient complained. This time the cysts were more marked on the anterior vaginal wall. The cysts continued to recur, and it was necessary to open them at intervals of four to six weeks in order to relieve the discomfort in the vaginal canal. Jan. 10, 1935, the patient had a spontaneous premature labor and delivered a five months' fetus which showed signs of heartbeat for thirty minutes but never breathed. The placenta contained a large hematoma. It was the obstetrician's opinion that the premature labor was due to an abruptio placentae. When she was examined six weeks postpartum no cysts were present, and all pelvic symptoms had subsided.

This patient was examined in September, 1936, and no traces of blebs were found.

LITHOPEDION

S. A. OSHEROFF, M.D., OMAHA, NEB.

(From the Department of Obstetrics and Gynecology, Creighton University)

MRS. D., aged twenty-eight years, came to see me on Feb. 28, 1935, with the following complaint: vaginal bleeding, commencing in the middle of December and continuing daily up until the present time, which has not been profuse at any time nor was it accompanied by pain. She passed a few small clots. Her menses had been regular and normal up until September. She missed her periods in October and November, started to flow in December and kept it up.

She had been married for ten years and had conceived and miscarried about nine years ago.

She stated that she had considerable pain in her right side during her pregnancy which was terminated after four months by a spontaneous abortion.

She had a rather prolonged convalescence, but in six weeks she was up and around attending to her usual household duties. However, the pain and tenderness in the right side continued, and lately she noticed a tender lump in her lower abdomen to the right.

The physical examination was negative, except for pale and anemic appearance. Cervix normal, uterus small, showing two nodules on the opposite lateral surfaces, a little above and to the left a large cystic mass could be felt, which was not tender, spherical in shape and extending upward to the superior spine of the ilium; it was slightly movable. On the right side of the uterus, about one inch medial to McBurney's point, there was another mass about the size of a large hen's egg, rather hard to the touch and quite tender, and it was somewhat fixed.

A diagnosis was made of fibrotic uterus, ovarian cyst on the left, possible pedunculated adherent fibroid on the right. She was sent to the hospital and operated upon on March 2, 1936. Under evipal and ether anesthesia the abdomen was opened in the midline. A hard calcified mass was found the size of a large hen's egg, firmly adherent to the omentum and fimbriated end of the right tube. It was lying anterior to the uterus and about three inches above and lateral to it. Upon palpation one could easily feel the grating of bones inside the calcified sack. The mass was removed without difficulty and was found to contain a fetal skeleton about the size of a four and one-half months' pregnancy.

On the left side an ovarian cyst, the size of a medium-sized grapefruit, was found with the tube distended and completely adherent to the cystic mass. This was also removed. The uterus was of normal size but contained fibrotic nodules at both cornua. As this made it useless from a reproductive standpoint, it was thought best to remove it and thus obviate the possibility of another operation if the fibroids should happen to grow.

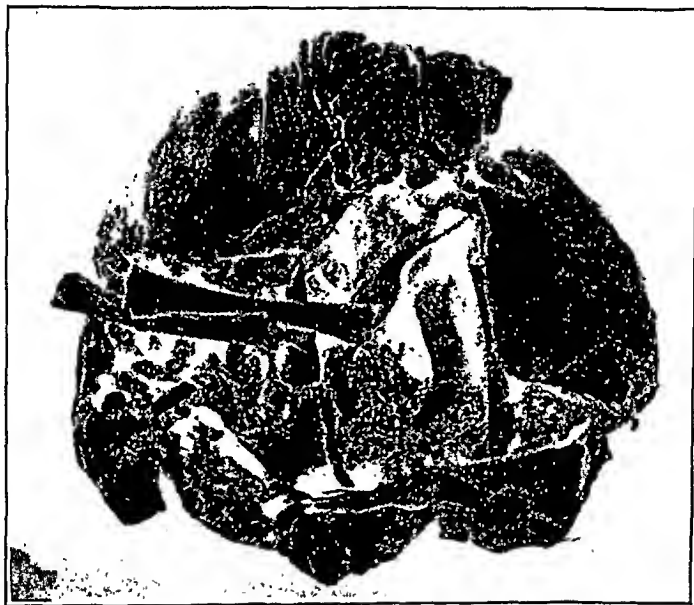


Fig. 1.

The right ovary looked fairly normal, and it was preserved. Prophylactic appendectomy was done. The abdomen was closed in the usual manner.

Histopathologic Examination: The tubal mass measured 6 by 5 by 5 by 4 cm. and had the feel of a cracked eggshell. On cut section it showed a lining of flat bone and contents of grayish yellow grumous material with numerous spicules of bone, having the appearance of long bones, tibia, femur, and humerus. The uterus measured 7 by 5.5 by 3 cm. showing marked hyperplasia of the lining and hemorrhagic at the cornua of the left tube. There was a small subserous fibroid at the right tube and a small chocolate cyst, having the appearance of an endometrial implant. The ovarian cyst with attached tube was 8 cm. in diameter, with thin walls and serous yellow fluid contents. *Microscopic:* The uterine wall was thickened and fibrosed. The mucosa showed marked hyperplasia and hypertrophy with twenty or more acini in the low power field. There was no evidence of any malignancy.

Diagnosis: (1) Benign hyperplastic endometritis, (2) lithopedion, and (3) simple unilocular cystadenoma of left ovary.

The postoperative course was uneventful, patient leaving hospital on the twelfth day.

In viewing this case in retrospect, it is evident that this was a case of right tubal pregnancy, occurring nine years previously, followed by abortion of fetus into the abdominal cavity, and formation of adhesions between fetal sac on one side and omentum and fimbriated end of tube, on the other, continued growth of fetus until the fourth month of gestation, with death and calcification following.

236 MEDICAL ARTS BUILDING

COLLECTING A CLEAN URINE SPECIMEN

B. H. CARROLL, M.D., TOLEDO, OHIO

DR. LITT* described the use of an adaptor for collecting urine from women under aseptic conditions. Any procedure which lessens the number of catheterizations is of great importance. In using the adaptor several disadvantages developed. The glass of an ordinary adaptor is fragile and easily broken. The pressure required in applying the adaptor about the opening of the urethra is often sufficient to prevent the act of urination. The presence of a nurse to hold the adaptor may defeat its purpose.



We have had an adaptor of similar size made up from Pyrex glass and therefore not easily broken.† A collar of soft rubber is fitted about the neck with a visor or shield 1 cm. long extending forward on the anterior surface to direct the flow of urine into the tube.

After cleansing the patient as for catheterization, the labia are separated and the adaptor with rubber collar is placed about the opening of the urethra. The labia are allowed to fall around or grasp the rubber collar and hold it in place. A small basin is placed for the urine as it comes from the adaptor. Proper draping should be arranged over the patient and the nurse may leave the room, if necessary.

*Litt: AM. J. OBST. & GYNEC. 39: 433, 1935.

†Made by Rupp & Bowman Co. Toledo, Ohio.

PREGNANCY AFTER THE REMOVAL OF BOTH OVARIES

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THE difficulty of devising any method for the certain sterilization of a patient is well recognized, but ordinarily it is thought that where both ovaries have been completely removed, future pregnancies will not occur. There are, however, a few cases on record where this is not true, and in 1902 Doran* reviewed previously reported cases and reported one of his own.

It may be noted that in most of the reported cases there was some difficulty in dissecting out the ovaries, and consequently there was a possibility that some normal ovarian tissue was left. There is always the possibility, however, that in these patients there is accessory ovarian tissue which possibly occurs more frequently than we are accustomed to think.

The case that I wish to report must be put down to the presence of unrecognized accessory ovarian tissue, as there was no possibility of any tissue being left from either of the normal ovaries. The patient was thirty-one years of age and had three normal full-term children. Ten months after her last confinement a solid tumor of the left ovary the size of an orange was discovered. During the next month this was obviously increasing in size and on Feb. 28, 1934, the abdomen was opened and this tumor was found to be a freely movable dermoid of the left ovary. At operation a dermoid of the right ovary the size of a lime was discovered which had not been felt previous to operation. It appeared to be impossible to leave any normal ovarian tissue and consequently both tumors, which were free from adhesions, were removed, the outer half of each tube being removed with the corresponding ovary. The tubal stumps and the pedicles were ligated with catgut. Six weeks after operation the patient developed well-marked menopausal symptoms, consisting of hot and cold flushes, nervousness and other evidence of vasomotor disturbances. These symptoms continued for about three months at which time the patient had a slight menstrual flow and the menopausal symptoms disappeared. Menstruation then continued at about six-week intervals until Jan. 15, 1935.

In May the patient returned for examination because there was no further menstruation and was found to be pregnant. This pregnancy progressed in an uneventful manner and the patient was delivered of a full-term child on Nov. 9, 1935. The baby was not nursed and menstruation has not recurred and the menopausal symptoms have returned to a slight degree.

At the time of operation no accessory ovarian tissue was seen, but it is obvious that it must have been present. It is of interest, however, that when the patient was examined on Jan. 22, 1935, before it was known that she was pregnant, a note was made of a small movable mass the size of a filbert low down in the right fornix. The note states that "this feels like a small ovary." It cannot be felt at the present time, March, 1936.

I believe that this case must be accepted as a pregnancy occurring from accessory ovarian tissue which did not at first function, but which after the removal of the other ovary gradually became functioning tissue.

*Doran, Allen: *Obstetrical Transactions* 44: 231, 1902.

CARCINOMA OF THE CERVIX IN PROLAPSED UTERI

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CARCINOMA of the cervix in association with procidentia is a very rare condition, as attested by Guthrie and Bache, who in 1932 made an extensive review of the literature, supplemented with a questionnaire sent to the leading clinics and gynecologists throughout the United States. They found not a single instance had been reported in the entire French literature nor had other outstanding European gynecologists seen a case. The late J. G. Clark, shortly before his death, stated that he had never seen the two conditions in the same patient. Judd of the Mayo Clinic saw three cases of cervical cancer out of 2,188 procidentias, while Graves saw only one case out of 683 patients. Pomtow reviewing the literature up to 1893 found only 29 cases recorded. There are probably not over 70 cases noted to date, and since all of these are not reported (most were elicited by questionnaire), there may be a certain amount of overlapping. I feel that this case is both rare and interesting enough to be noted, as it represents the only case that I have encountered in the 700 consecutive cervical cancers personally observed.

Mrs. A. S., a Swedish widow of seventy-six years, was admitted to the Clinic on May 4, 1934, complaining of leucorrhea and vaginal bleeding for the past six months, and a "fallen womb for nine years." The menopause occurred twenty-six years ago. The patient had had four full-term spontaneous deliveries. The pertinent physical findings were mitral and aortic stenosis, associated with a mild hypertension. Vaginal examination revealed a complete procidentia. The cervix at its most dependent portion presented an ulcerated, eroded area measuring $3 \times 3\frac{1}{2}$ cm. which was firm in consistency and bled on manipulation. This ulcerated area was surrounded by a zone of induration.

At this same visit, a biopsy was taken which revealed on microscopic examination changes in the prickle cell layer of the epidermis, with an unrestrained growth of cells. The neoplastic cells occurred as large compact masses, some of which were undergoing degenerative changes, presenting cystic-like formation. Clumps of these cells were observed within lymphatic channels. There was a slight tendency toward keratinization. The stroma was the seat of leucocytic infiltration.

Diagnosis: Prickle cell carcinoma.

Through some oversight the patient was admitted to the hospital twenty days later without any radiation at all and had a vaginal panhysterectomy done. Report of the specimen confirmed the original biopsy findings. The patient was discharged from the hospital on the thirteenth day, after an uneventful convalescence, except for a vesicovaginal fistula, which occurred at the operation. Follow-up a year and a half later revealed the vaginal vault to be high, free from any malignant recurrence, with a persistent fistula which the patient refused to have corrected.

This case is reported through the courtesy of Dr. John J. Guincy.

755 OCEAN AVENUE

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

THE MEDICOLEGAL ASPECTS OF BLOOD GROUPING

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THE discovery of the blood groups in 1900, 1901 by Karl Landsteiner^{1, 2} not only made blood transfusion—hitherto a therapeutic fantasy—a feasible and valuable procedure, but also opened up a completely new field in blood research, which in the short space of a year yielded its first medicolegal fruits. Thus, in 1902, Landsteiner and Richter³ demonstrated the possibility of identifying the blood groups from bloodstains, and of applying this knowledge in those cases where bloodstains of either the criminal or victim had been left at the scene of a crime.

In 1910, von Dungern and Hirszfeld⁴ demonstrated the hereditary nature of the four blood groups, and advocated the application of this knowledge in forensic cases for the exclusion of paternity. According to these workers the agglutinogens A and B were transmitted as Mendelian dominants, by two independent pairs of allelomorphic genes, so that the agglutinogens could not appear in the blood of a child unless present in the blood of one or both of its parents.

The inheritance of the blood groups has been corroborated by all subsequent workers, but in 1925, Bernstein⁵ proposed a new theory of transmission which conformed much more closely with statistical expectancies and with the data which had accumulated during the preceding period of fifteen years. This theory is now universally accepted. According to Bernstein's theory, the blood groups are inherited by means of three allelomorphic genes, A, B, and R. This theory supplies another postulate which is important for the exclusion of paternity, namely, that a group AB parent cannot have a group O child, and a group O parent cannot have an AB child, a situation which could occur were the von Dungern and Hirszfeld theory correct.

By this time the legal machinery had been started on the continent, and through the work of Schiff in Germany and Lattes in Italy, the isoagglutination tests were gradually being accepted in the courts as evidence in cases of disputed paternity. According to statistics compiled by Schiff,⁶ by 1929 the tests had been used in as many as 5,000 cases in the various countries of Europe.

Meanwhile, further developments had taken place in the serologic phases of blood grouping. In 1911, von Dungern and Hirszfeld⁷ had succeeded in demonstrating that there are two sorts of agglutininogen

A, subsequently designated A_1 and A_2 by Landsteiner and Levine. With their aid, the individual differences in human blood were increased to six, namely, O, A_1 , A_2 , B, A_1B and A_2B , so that the possibilities for criminal identification were greater. Although the hereditary nature of the subgroups of Group A and Group AB is now generally recognized, certain technical difficulties make their forensic application unsafe for the time being.

The discovery by Landsteiner and Levine in 1927^{8, 9} of the M and N properties of human blood and the fact that these, too, were inherited gave further impetus to the new branch of forensic medicine, and by 1932, this knowledge was being applied in European courts. Up to that time, although a large part of the pioneering in this field of research had been done in America, its recognition as a reliable criterion in forensic medicine was confined almost exclusively to European countries. In 1930, the famous Bamberger-Watkins case occurred in Chicago.¹⁰ In this case the accidental interchange of two newborn infants in a hospital, rectified by the use of the blood groups, did much to focus the attention of both the medical and legal professions on the possibilities of these discoveries. The next case occurred in New Haven in 1933,¹¹ and this time the blood groups were used successfully to effect an exclusion of paternity. Progress was slow, however, and certain legal difficulties still barred the way to universal adoption of the test.

In 1934, at a meeting of the American Medical Association, following an address by Karl Landsteiner,¹² a resolution was passed to acquaint the legal profession with the reliability of these tests, so that steps might be taken to facilitate their application in forensic cases. Hitherto, this type of evidence was admissible, but the courts did not have the authority to compel the parties in an action to submit to the examination against their will.¹³ On March 22, 1935, laws were passed in New York State giving the courts of that state the power to order blood tests in cases where the question of paternity or maternity was relevant to the issue. Shortly thereafter similar laws were passed in Wisconsin, and probably the other states will follow suit. According to the existing laws in New York State,¹⁴ the defendant in a paternity proceeding now has the right to demand a blood examination to establish his innocence.

The results of such tests are of value only for purposes of exclusion, as when a particular combination of blood types in the putative father, mother, and child is incompatible. On the other hand, compatibility is of no positive value. Because of the limited number of blood types, there is a possibility of coincidence. For example, the falsely accused man and the father could belong to the same blood type. In Wisconsin¹⁵ the statutes are so framed that evidence based on blood grouping is admissible only if an exclusion of paternity or maternity is definitely established. As stated before, the Bernstein theory postulates that the blood groups are transmitted by three allclomorphic genes. Corresponding to the four blood groups, six genotypes are possible (see Table I). On this basis, it is a simple matter to deduce what groups are possible in the children, when the groups of the parents are given. For example, if the father belongs to Group AB, and the mother to Group O, half of the sperm will carry gene A, and half gene B, whereas all the ova will carry the gene R. Equal num-

TABLE I. BERNSTEIN'S THEORY OF HEREDITY OF THE BLOOD GROUPS

PHENOTYPE	GENOTYPE	
	HOMOZYGOUS	HETEROZYGOUS
AB		AB
A	AA	AR
B	BB	BR
O	RR	

bers of zygotes must be of genotypes AR and BR, so that half of the children will belong to Group A and half to Group B. In a similar manner, the other nine matings possible can be analyzed (see Table II).

TABLE II. THE BLOOD GROUPS IN PARENTS AND CHILDREN

GROUPS OF PARENTS	GROUPS OF CHILDREN POSSIBLE	GROUPS OF CHILDREN NOT POSSIBLE
O × O	O	A, B, AB
O × A	O, A	B, AB
O × B	O, B	A, AB
A × A	O, A	B, AB
A × B	O, A, B, AB	—
B × B	O, B	A, AB
O × AB	A, B	O, AB
A × AB	A, B, AB	O
B × AB	A, B, AB	O
AB × AB	A, B, AB	O

A study of Table II shows that: (1) The agglutinogens A and B cannot be present in the blood of the offspring unless present in the blood of one or both parents. (2) An AB parent cannot have an O child. (3) An AB child cannot have an O individual as one of its parents. As an ancillary test, Schiff¹⁶ has pointed out that if the corpuscles of the infant are agglutinated by the serums of both parents, then nonpaternity is established, except in the case where the child is of Group AB and the parents of Groups A and B, respectively.

Since the possibility of distinguishing two genotypes depends on the relative frequency of all genotypes in the population, and this frequency varies in different localities, the chance of effecting exclusion of paternity also varies in different localities. Wiener¹⁷ has shown that, using the four blood groups, the chance of effecting an exclusion of paternity ranges between 16 and 19 per cent for most localities. These figures refer to the chance of excluding paternity if the defendant is actually innocent. In actual practice, however, the percentage is lower, since many of the defendants are not entirely blameless. If the individual, unjustly accused, belongs to the Group AB, he has two chances in five of proving his innocence. The individual of Type O comes next with one chance in five. The B type is less fortunate, with only one chance in seven, whereas the A individual is truly unfortunate, should he be falsely accused of paternity, since his chances are only one in thirteen.

If only one of the parents is available, a serologic examination of his or her blood and that of the child may yield pertinent information, but naturally the chances are less than when both parents are tested. This circumstance may arise, for example, in cases where the husband suspects infidelity, but prefers to gather further evidence before con-

fronting his wayward spouse; or when one of the parents is dead. If the man or woman is shown to belong to Group AB and the child to Group O, or the supposed parent to Group O and the child to Group AB, parentage is immediately excluded.

With the discovery of the M and N properties of human blood, the serologist's scope was further increased. The agglutinin N has no natural agglutinin, and only one case has been described in which natural agglutinins for M were present in human blood.¹⁸ Antiserums can be prepared, however, by immunizing rabbits with M and N blood. From these, testing fluids are made which give specific agglutination reactions for M or N, similar to those of the blood groups A and B.

The agglutinogens M and N are inherited as simple Mendelian dominants, by means of a single pair of allelomorphic genes, M and N. The following genotypes are, therefore, possible: MM, NN and MN, corresponding to the three known types M, N and MN, respectively. By reasoning, similar to that used for the blood groups, one can determine to what type or types the children from any mating must belong (see Table III).

TABLE III. THE HEREDITY OF MN TYPES OF LANDSTEINER AND LEVINE

MATINGS	GROUPS OF CHILDREN POSSIBLE	GROUPS OF CHILDREN NOT POSSIBLE
M × M	M	N, MN
N × N	N	M, MN
M × N	MN	M, N
M × MN	M, MN	N
N × MN	N, MN	M
MN × MN	M, N, MN	—

From Table III it follows that: (1) The agglutinogens M and N cannot appear in the blood of the child unless present in the blood of one or both parents. (2) Two parents belonging to Type M cannot have Type N children, and parents of Type N cannot have Type M children. The frequencies of the three types in the general population are approximately: M, 30 per cent; N, 20 per cent; and MN, 50 per cent. An innocent man of Type M or N has about one chance in three of clearing himself, whereas the MN type has no chance whatever. A falsely accused man of undetermined type has approximately one chance in six of proving nonpaternity by exclusion. By combining the blood groups and MN types, the chances of disproving paternity have been increased to one in three.

The following case illustrates how this knowledge can be applied.*

In September, 1935, a woman in Buffalo, New York, sued her husband for separation, while he countered with a suit for annulment of marriage on the basis of fraud. The facts were that up to the time of the trial she had been in the state of matrimony seven times. During the sixth venture, she had had an affair with her present husband, and the child in question was supposed to be the fruit of that clandestine union. However, the defendant denied that the child was his; in fact, he asserted that it was not even his wife's, insisting that he had been inveigled into his marriage by that pretext. In the court it was shown that the child and putative father both had a "curly large toe," and the plaintiff's counsel made capital of

*I am indebted to Dr. A. S. Wiener for the details of this unpublished case.

this observation. Eventually a blood test was ordered by the court, and the following results were obtained: mother, AN; putative father, BM; and the child, BM.

From this it can be seen that the woman could not possibly have been the mother of the child. This conclusion is based upon the law that a Type N parent cannot have a Type M child, the result of the classic blood grouping tests being inconclusive. Incidentally, evidence was presented at the trial to show that the plaintiff had had a salpingectomy and an ovariectomy performed in 1916. The woman explained her midline scar by asserting that she had had her present child by cesarean birth, although she could not produce the surgeon who was supposed to have performed the operation. However, the former husband testified that the plaintiff had not been pregnant at the time the child was born; in fact, she had never menstruated as long as he knew her. Finally the true father was located, and it was learned that he had left the child at the same orphan asylum from which the plaintiff had adopted it.

Here is a case of a carefully planned fraud which might have succeeded had it not been for the use of the blood grouping tests.

Experience over a period of twenty-five years has shown that these tests are completely reliable in the hands of the expert serologist. Since the fate of several people depends upon the decision, it is essential that the person performing the tests be well experienced in the technic. For this reason, the court should permit only physicians appointed by authoritative medical councils with expert genetical advice to undertake the examinations.

As mentioned before, there are two sorts of agglutinin A, namely, A_1 and A_2 . The agglutinin A in Subgroups A_2 and A_2B reacts more weakly than the corresponding agglutinin in Subgroups A_1 and A_1B . The agglutinin is not infrequently so weak in Subgroup A_2B , that errors may result in inexperienced hands. As a rule, the weaker types are readily recognized, but when the sensitivity of the corpuscles is less than usual, and a serum of low titer is used, the reaction will be missed. Therefore, it is essential to use only serum of high titer, using both A_1 and A_2 blood as controls. By doing each test at least in duplicate, using different serums for each set-up, the chances of error are further minimized. As an additional control the unknown serums should each be tested against known cells of Groups O, A_1 , A_2 and B.

The agglutinogens are already present in the blood of the child at birth, and whatever agglutinins are present in the serum were derived from the mother by filtration through the placenta. During the first few weeks of life, these agglutinins gradually disappear to be replaced by the permanent agglutinins of the individual. *Pari passu* with these changes the sensitivity of the agglutinin increases, until it reaches its maximum strength in early adult life. It is evident, therefore, that it is unwise to apply these tests too early in life, particularly if the child belongs to either Group A_2 or A_2B . In competent hands, however, a reliable result can be obtained as early as the second week of life.

Recently, Friedenreich¹⁹ demonstrated the existence of a rare type of N agglutinin, designated by him as N_2 . This type is very much weaker than the common agglutinin N, designated by Friedenreich as N_1 . The agglutinin N_2 is especially weak in the presence of M, so that blood MN_2 could be wrongly diagnosed as M. Due regard to the precautions previously outlined is the only way of avoiding this pitfall.

In conclusion, it should be pointed out that proper precautions should be taken to identify the individuals presenting themselves for the test. Whenever possible, the plaintiff and the defendant should identify each other before the samples of blood are taken. In addition, some permanent record should be kept, either by means of photographs or fingerprints, in order to forestall any attempt at substitution.

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Lesnoi, S. K.: Disorders of Menstrual Function Due to Atresias and Cervical Stenosis After Induced Abortion and Operative Delivery. Vopr. Endocrinol, Moskow, p. 913, 1936.

The trauma inflicted during the performance of an artificial abortion leads at times to the firm concentric and excentric atrophy of the uterus. Some writers see the danger in a hormonal trauma, due to interruption of the trophic influence of the corpus luteum hormone. After spontaneous termination of pregnancy or instrumental delivery, such menstrual disturbances as hypomenorrheas and amenorrheas may be due solely to local, mechanical traumatization of tissues. Traumatization by a sharp curette affects the uterus itself, and most frequently the region of the internal os. Pathologico-anatomic studies of Stieve disclosed that the cervix may acquire a structure resembling that of cavernous bodies, the connective tissue becomes friable, the muscular elements and the glands proliferate, and the venous system develops. It appears that even a relatively small obstacle may prevent the natural flow of fluid contents from the uterine cavity.

Reporting 22 cases, the author states that instrumental damage leads to the formation of adhesions and scar tissue in the cervical canal, and often results in stenosis or even atresia of the canal. In all patients with hypomenorrhea and amenorrhea, developing soon after artificial abortion and delivery with operative interference, it is necessary to see whether a uterine sound can be passed through the cervical canal. In recent cases it is sufficient to dilate the cervical canal once with Hegar dilators up to No. 7. In neglected cases repeated dilatation is required. In some instances it is necessary to excise the obstacle and then follow with repeated dilatations. Neglected cases require also hormonal therapy.

ALEXANDER GABRIELIANZ.

*Details of technic.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

Meeting of May 12, 1936

The following papers were presented:

Comparative Study of Pelvic Temperatures Under Various Therapeutic Procedures. Dr. Harold C. Ingraham. (For original article, see page 1048.)

A Review of 226 Cases of Obstetric Analgesia. Dr. Virgil G. Damon (by invitation). (For original article, see page 1009.)

Therapeutic Abortion by Means of X-ray. Drs. Max D. Mayer, William Harris, and Seymour Wimpfheimer. (For original article, see page 945)

CHICAGO GYNECOLOGICAL SOCIETY

Meeting of March 20, 1936

The following case reports and papers were presented:

Two Cases of Unruptured Ectopic Pregnancy. Dr. Milton M. Scheffler. (For original article, see page 1061.)

Hemorrhage Into a Fibroid During Pregnancy. Dr. Wm. H. Browne.

A Biologic Test for the Diagnosis of Intrauterine Fetal Death. Dr. George H. Rezek. (For original article, see page 976.)

The Surgical Treatment of Puerperal Sepsis. Dr. A. F. Lash.

A Critical Study of the Low Cervical and Classical Cesarean Section Operation. Dr. Frederick H. Falls. (For original article, see page 989.)

BROOKLYN GYNECOLOGICAL SOCIETY

Meeting of March 6, 1936

The following paper and case report were presented:

Carcinoma of the Body of the Uterus. Dr. C. C. Norris and Dr. F. S. Dunne. (For original article, see page 982.)

A Full-Term Pregnancy Complicated by an Acute Intestinal Obstruction and False Labor Pains. Dr. John Casagrande. (For original article, see page 1058.)

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Pathology of Labor

Brown, R. Christie: The Treatment of Obstetric Disproportion, Brit. M. J. 1: 1251, 1935.

Recognition of the presence of disproportion is difficult, yet most important. Major disproportions are easily recognized by the ordinary methods of measurement, which reveal marked pelvic contraction. They all require cesarean section. In cases of minor disproportion the x-ray offers an additional aid to diagnosis, but the outcome of labor in these cases is uncertain, and a decision can be made only after a test of labor. This applies especially to primiparas. Pelvic measurements alone are not a criterion; they must be considered in conjunction with all other factors when giving the prognosis, i.e., the size of the fetal head, general build of the patient, age of the patient, mobility of pelvic joints, presentation, course of first stage, force of uterine contractions, fortitude of the patient, and the molding of the head.

A vaginal examination is advocated in every case during pregnancy and after membranes rupture during a test of labor. Induction of premature labor for disproportion has no place in the delivery of a primipara, but it may be useful in the delivery of a multipara whose record of a former labor has been carefully kept and can be used as a guide to the ability of the patient to deliver herself. In minor disproportions only a test of labor will estimate the patient's chances for delivery which no amount of skill can lead an observer to decide upon during pregnancy. In all cases of doubt, in the primipara, the patient should be allowed to go into labor spontaneously at term and the labor be observed. In this way an accurate opinion can be arrived at during the first stage.

F. L. ADAIR AND S. A. PEARL.

Pettit, Garland, Dunn, and Shumaker: Correlation Between the Shape of the Female Pelvis and the Clinical Course of Labor, Western J. Surg. Obst. & Gynec. 44: 1, 1936.

Applying the roentgenologic technic and the classification of pelves elaborated by Caldwell and Moloy in a series of 100 consecutive labors, the authors conclude that the classification of pelves on an architectural basis by roentgen methods is a simple and clinically feasible procedure, and that in a significant number of cases a difficult labor can be forecast by pelviography in patients whose obstetric measurements by ordinary methods appear normal. This is especially evident in the android group.

HUGO EHRENFEST.

Mann, John: The Mechanism of Rotation in Occipito-Posterior Positions, *Canad. M. A. J.* 33: 607, 1935.

The author reviews and discusses various factors concerned with the mechanism of rotation in occipitoposterior positions. Mention is made of the size and shape of the maternal pelvis in relation to the maximum available diameters, and the usual theories are discussed. Positions and degrees of flexion of fetal heads are used to explain failures of rotation. The idea is advanced that the fetus himself is responsible for some rotation of his head. Analgesic drugs that do not interfere with the force of uterine contractions are satisfactory and may be used liberally. In prolonged first stage, membranes should remain intact but after complete dilatation they should be ruptured.

A general discussion of various treatments follows, after which the author describes his universal joint forceps and their use. He does not present any data or statistics.

H. CLOSE HESSELTINE.

te Groen, L. J.: Vertex Presentation With Extended Head, *South African M. J.* 9: 305, 1935.

Two causes for this condition are offered: the large, wide pelvis and the flat pelvis. The term "sincipital presentation" is adopted. In South Africa it is seen most commonly in women with large, wide pelvises, and where the baby has a round head.

The mechanism of the development of the attitude is described. A round fetal head and a wide pelvis with little resistance lead to this attitude in multiparas when the head is high above the brim and begins to enter the pelvis only when labor is well advanced, and where the membranes had ruptured with early pains.

Posture of the patient is given as a factor in influencing presentation. The author believes that where the baby's back is on the right and the patient lies on her left side, the descent of the head will encourage sincipital or even brow or face presentations. Amsterdam teaches to allow the patient to remain on the same side as the back of the baby in normal pelvises, and on the opposite side in cases of flat pelvis.

In sincipital presentations the large fontanel is readily felt. The mechanism of labor is akin to that of a brow presentation, except that in the latter the maxillary fossae engage under the symphysis, whereas in the sincipital form the root of the nose is under the symphysis.

F. L. ADAIR AND S. A. PEARL.

Kawakami, H.: Application of "Atonin" in the Clinic, *Jap. J. Obst. & Gynec.* 17: 326, 1934.

The Japanese preparation of pituitary extract is known as "atonin." Kawakami used this drug in about 200 patients during every stage of labor. In the first stage of labor he injected varying doses up to 0.5 c.c. However, he suggests that not more than 0.3 c.c. be used during labor. He found that atonin was followed by such complications as: rupture of the perineum, fetal asphyxia, and cerebral hematoma. There were more of such complications among patients who received atonin than among those who did not. Furthermore, the complications were proportional to the dose used. The higher the dose the more frequent the complications. The author found the drug very useful for postpartum hemorrhage. He prefers subcutaneous injection to the intravenous use.

J. P. GREENHILL.

Riley, P. W. S.: Obstructed Labour, New Zealand M. J. 34: 119, 1935.

A case of obstructed labor due to a pelvic kidney is reported. True nature of case was revealed only at operation. A unilateral, lobulated, single kidney was lying in the true pelvis and to the right. No kidney was palpable on either side of the lumbar region. Pyelogram confirmed the singularity of the organ. It was a congenitally misplaced kidney, said to be more common in women. Patient had no structural genital defects or leakage of urine indicating an aberrant ureter.

F. L. ADAIR AND S. A. PEARL.

Katsu, Y.: A Newly Discovered Symptom for the Diagnosis of Anencephalus, Jap. J. Obst. & Gynec. 15: 507, 1932.

Usually the diagnosis of anencephalus is made before delivery on the following vaginal findings: (1) palpation of spongy soft tissue surrounded by projecting cranial bones, (2) abnormal protrusion of the eyeballs, (3) palpation of bony protuberances such as the sella turcica or the foramen magnum, (4) abnormally small head, and (5) difficulty in obtaining ballottement due to an abnormally short neck. In addition to these findings the x-ray examination supplies confirmatory evidence as does also Negri's sign. According to the latter sign, if pressure is made on the cerebral substance at the base of the skull, the fetus responds with a violent motion or with spasmodic movements. The author in two cases found that pressure on the cerebral substance also produced a sudden and definite slowing of the fetal heart rate. Release of the pressure resulted in a normal heart rate.

J. P. GREENHILL.

Ahlthrop, G.: A Contribution to the Diagnosis of Anencephalus Before Delivery, Acta obst. et gynec. Scandinav. 13: 93, 1933.

Ahlthrop describes a case of anencephalus in which the diagnosis was made before delivery. The diagnosis was based chiefly on the circumstance that the fetal movements were especially lively at every rectal palpation on the presenting head of the fetus. This symptom, first described by Laulaigne, seems to have been subsequently overlooked as an indication of anencephalus. The diagnosis was verified by x-ray examination.

An unmistakable diagnosis can be obtained by radiography. This has been done in more than 40 cases up to the present time.

X-ray examination to ascertain the possible presence of an anencephalus is indicated under the following conditions: (1) when the fetal head cannot be surely palpated; (2) in hydramnion, with the possibility of twins excluded; (3) when there are vigorous fetal movements during palpation of the suspected presenting part.

J. P. GREENHILL.

Porcardo, Diago: A Sign of Orientation in the Diagnosis of Anencephalus, Ginecologia (Torino) 1: 845, 1935.

The author calls attention to a sign easy to verify in the anencephalus. It consists in the rapid movements of the presenting part (face presentation), but particularly of the mouth to the point of squeezing the finger introduced in it.

AUGUST F. DARO.

Laubscher, A. E.: Methods of Terminating Labor, South African M. J. 9: 222, 1935.

An outline of the physiology and mechanism of the onset of normal labor is presented, which is summarized as "a number of stimulants with cumulative effect

are brought to act on a suitably prepared uterus and thereby influence the uterus in such a way that it starts contracting rhythmically. . . . Pressure of the presenting part on the lower uterine segment plays its part in the determination of the frequency and severity of the pains."

Methods advocated are dilatation of cervix and blunt curette in the early months, using great caution not to perforate uterus. In later months, between third and seventh, vaginal hysterotomy is advised for skilled operators. After the seventh month induction is by drugs: castor oil, quinine, and pituitrin.

Rupturing the membranes is a dangerous procedure. The author alludes to the use of the stomach tube in the uterus and to the use of the metrorrhyster; the latter is more certain of producing dilatation.

F. L. ADAIR AND S. A. PEARL.

Stacey, J. Erie: Analgesics in Labour, Brit. M. J. 1: 817, 1935.

The author approaches the subject of analgesia in labor from the standpoint of relief of pain for the whole of labor. So little is known of the mechanism of pain that he feels we have no scientific basis for relieving its symptoms. An impoverished blood supply to muscles will elicit pain due to a local production of a chemical material called "p" substance. For practical purposes the author feels that a proper attitude toward labor on the part of the mother and confidence in her accoucheur are the most important factors in the relief of pain. Next, the choice of drug or anesthetic is of prime importance.

For the first stage he has great success with chloral (30 or 40 gr.) with or without potassium bromide in 4 or 6 ounces of water or glucose. This is repeated in one hour. It tides the patient over to the period when morphine may be safely given. Hyoscine used with morphine, he feels, needs a constant attendant.

He gives 1/100 gr. of hyoscine repeated in three-fourths hour, two hours later, and again three hours later depending on the reaction on the patient. In primiparas he starts this treatment when the cervix is taken up and the os is from 3 fingers to 1½ dilated, and the pains are ten minutes or less apart and of fifteen to thirty seconds' duration.

He enumerates the advantages of hyoscine as (1) simple of administration, (2) rarely produces hyperexcitability, (3) it produces forgetfulness of pain, (4) it does not cause uterine contractions to decrease, (5) the infant does not suffer from oligopnea, (6) the third stage is not prolonged, (7) postpartum hemorrhage is nil. Morphine he considers one of the most, if not the most, valuable analgesic in labor.

Of other analgesics he found Gwathmey's methods tedious and not always effective. He has not had much experience with the barbiturates except nembutal which produced pallor and coma in one or two patients and alarmed him. The author finds no better analgesic in the second stage than chloroform, or gas and oxygen. He thinks chloroform safe and uses it routinely. He uses gas in selected cases.

F. L. ADAIR AND L. G. COON.

Wachenfeldt, S.: Studies on Deliveries Among Multiparas, Acta obst. et gynec. Scandinav. 15: 1, 1935.

In the Woman's Clinic at the University of Lund from 1911 to 1930, there were observed 11,990 pregnancies which resulted in the birth of children weighing 2,500 gm. or more, in multiparous women. The duration of labor averaged about ten hours. It was shortest in women who had had 2 or 3 children but rose with further increase in parity. The frequency of head presentations diminished with increase in parity, whereas transverse presentations tended to rise in frequency

with increase in parity. Breech presentations occurred with equal frequency among all the patients. As parity increased the weight of the children of both sexes increased.

Placenta previa increased with increase in parity. There did not seem to be any change in the incidence of the toxemias of pregnancy. There was, however, a greater predisposition to preeclampsia and eclampsia as the age of the patient increased. Abruptio placentae definitely increased with increase in parity as did also diseases accidental to pregnancy. Postpartum hemorrhage increased in frequency with increase in parity, but puerperal infection tended to decrease in frequency.

There was no difference in mortality between the primiparas and multiparas, but the death rate of the children showed a marked rise among the multiparas.

J. P. GREENHILL.

Healy, T. M.: Observations on the Results of Operative and Spontaneous Deliveries, Irish J. M. Sc. 6: 543, 1934.

An increasing incidence of operative interference during pregnancy and labor is revealed in the publications from almost all maternity centers. The obstetrician of today, working in a well-equipped hospital as a member of a team, rejoices in the knowledge that he can show better statistics in his operative cases than were obtained when surgical intervention during parturition first became fashionable. Whether he has fewer fatalities to his discredit after a decade or two in practice, is more open to doubt; for in his enthusiasm for manual dexterity he is in danger of losing sight of the fact that he has yet to achieve results which will bear comparison with those of the spontaneous deliveries he so frequently cuts short. If we justify our operations by pleading that modern civilization has produced women who cannot deliver their babies, it seems arrogant to assert that the same generation has begotten a race of obstetricians to make good the failures.

WM. C. HENSKE.

Hirst, J. C.: Active Versus Conservative Management of Planned Deliveries, Am. J. M. Sc. 190: 806, 1935.

Conservative ward obstetrics is safest for mother and child; but reasonable assistance by a trained specialist yields as good results with more relief. Internes should be preinstructed in proper methods of delivery and the importance of rigid adherence to technic, and must be supervised in every abnormal labor and in all operative deliveries. A member of the major obstetric staff should be present at all operative deliveries other than outlet forceps, and at all breech deliveries. No effort whatever should be made to interfere with natural birth for the purpose of exhibition to students, since demonstration forceps or other operative deliveries instituted only for instruction of students or internes have been found unjustifiable.

J. THORNWELL WITHERSPOON.

Robiolis: Reflections on the Delmas Procedure, Bull. soc. d'obst. et de gynéc. 24: 582, 1935.

After having performed the Delmas method of forcible dilatation of the cervix under spinal anesthesia twelve times, the author stopped to analyze his results. The first patient died four hours after labor but the baby remained alive. The second patient was in a precarious condition for three hours after delivery. The same held true for the third patient who had an extensive postpartum hemorrhage. The fourth patient suffered an extensive hemorrhage from the left side of the

vagina and the cervix. The fifth and sixth cases had no complications. The seventh patient had repeated hemorrhages which finally necessitated a vaginal hysterectomy. The eighth patient had a severe laceration of the cervix. The ninth patient died, three hours after delivery of a dead baby, without any signs of hemorrhage. The tenth patient suffered from severe headaches. The eleventh patient had a serious cervical laceration. The twelfth patient was critically ill for eight hours after delivery and had to be transfused although there was no hemorrhage. On the basis of this experience the author feels that the Delmas procedure should be used only in rare cases when it is impossible to deliver a baby by any other means. It should be performed only in a hospital where preparations should be at hand for possible complications. The patient must be closely watched for at least five to six hours after delivery.

J. P. GREENHILL.

Rucker, M. Pierce: Obstetrical Shock, Virginia M. Monthly 62: 254, 1935.

Obstetric shock may be divided into three groups: (a) that due to hemorrhage; (b) other conditions well recognized as causing shock that may be concomitant with labor such as ruptured appendix, perforating gastric ulcer, ovarian cysts with twisted pedicle, etc., and (c) shock with no discoverable cause. The author quotes 15 instances of obstetric shock with no discoverable cause in a series of 7,177 cases of abortions and full-term labors. He suggests as possible cause of this type of shock the spill of blood or fluid into the peritoneal cavity through the fallopian tubes. It seems noteworthy that among the 15 cases reported by him there was only one of unaided delivery.

EUGENE S. AUER.

Wahl, F. A.: Sequelae in Children Born After Tribrom-Ethanol (Avertin) Anesthesia, Arch. f. Gynäk. 157: 17, 1934.

The use of tribrom-ethanol is of serious consequence to the babies that are born under the influence of this drug. Over 50 per cent show marked asphyxia even hours after delivery. In addition, over one-half are markedly apathetic, have a weakened cry, or rather whimper, nurse very poorly, and therefore have a marked increase in frequency and amount of aspirations and show a disturbed weight curve. From the fetal point of view, therefore, this method of anesthesia should be vigorously condemned.

RALPH A. REIS.

Atlee, H. B.: Evidence in Favour of a More Active Puerperium: A Study of 500 Cases, Canad. M. A. J. 33: 144, 1935.

In a study of the results of physical activity in the puerperium, the author finds some evidences to refute the more common idea that the puerperal woman should be inactive.

On the day following delivery the patient sits up in bed, but when reclining should be on her sides and abdomen. The leg, arm, and body exercises are gradually instituted beginning on the second day. On the fourth day the patient sits in a chair by the side of the bed. These activities are reserved for the normal cases and those having had forceps delivery and perineal repairs. If the patient objects, she is not forced, and if a fever develops she is restricted to bed rest.

The tables indicate that with a more active puerperium involution is not impaired, prolapse is not increased, the lochia disappear more quickly, infections

and embolisms are not increased, and the patients are able to take up their household duties earlier and with more zest. However, this series consists of only 500 cases.

H. CLOSE HESSELTINE.

Moir, Chassar: The Merits and Demerits of Oxytocic Drugs in the Postpartum Period, *Proc. Roy. Soc. Med.* 28: 1654, 1935.

Oxytocic substances are administered during the puerperium for three reasons: (1) To prevent atonic hemorrhage, (2) to check uterine hemorrhage, and (3) to promote involution.

As far as the writer knows there is no direct evidence that *involution* is aided by such drugs. Stopping indiscriminate routine use of these drugs in his services, in his belief, has saved nurses much unnecessary work, patients much inconvenience and nausea, the hospital a good sum of money, and as far as could be seen the uteri involved just as they had done before. Misuse of ergot may lead to *gangrene* of the extremities. The *effect of oxytocic drugs* can be recorded either by the Bourne and Burn's method (water filled bag in uterus connected with manometer) or Dodek's instrument recording changes in uterine shape through abdominal walls. In his own studies the writer found the latter method entirely sufficient for the purpose.

Glycerin, injected into uterus through a catheter, is an unreliable method of stimulating uterine contractions. *Gravitol*, a proprietary drug claimed to have ergot-like action, injected intramuscularly has a relatively feeble effect for about twenty minutes. *Histamine* (on the market under the trade name "ergamine") cannot be given in a dose large enough to be therapeutically effective without also producing undesirable by-effects. It is unsuited for any obstetric emergency. *Ergotoxine* and the almost identical alkaloid *ergotamine* (trade names *femergin* or *gynergen*) are now freely used. Other ergot alkaloids more recently isolated are *sensibamine* and *ergoclavine*. All four make a well-defined group in regard to their clinical action which is practically the same. They have large molecules and, perhaps because of this, are slow to take effect when administered in permissible dosage. When given by mouth no effect is seen in graphic recording before thirty-five minutes have elapsed. Resulting uterine contractions are small and erratic. It seems possible that repeated oral administrations may lead to a prolonged heightened irritability of the uterus. Administration of members of this group by intramuscular injection is a more satisfactory procedure. After about twenty minutes strong contractions gradually set in which soon merge into a uterine spasm, followed by strong isolated contractions for several hours. The new alkaloid *ergometrine* in several respects contrasts to those already mentioned. Clinically and pharmacologically it must be placed in a class by itself. It is remarkable for its rapidity of action. It works by mouth usually in five to eight minutes, by intramuscular injection in three to four and a half minutes, by intravenous administration in about one minute. There is a uterine spasm which lasts for about an hour and is followed by strong regular contractions for one and a half to three hours. Clinically the ergotoxine-ergotamine group is distinctly inferior to ergometrine, though the spasm of the first group, setting in later, lasts longer.

There follows a consideration particularly of posterior pituitary extracts in the prophylaxis of postpartum hemorrhage. The purified pitocin, largely freed of the pressor principle, is preferable to the usual preparations especially in cases of obstetric shock. Pituitary extract for long has been the sheet anchor in treating postpartum hemorrhage on account of its rapid and intense action, but the new ergometrine now is a serious rival, especially when administered intravenously. Its use is not contraindicated by obstetric shock.

HUGO EHRENFEST.

Naljawinsky, W.: Uterine Ruptures, *Monatschr. f. Geburtsh. u. Gynäk.* 98: 167, 1934.

Among 6,367 labor cases at the Second Moscow Woman's Clinic, there were 15 cases of uterine rupture. One of these women had a rupture of the uterus twice. The author found that rupture of the uterus occurred much more frequently in multiparas than in primiparas. Symptoms of rupture may be entirely absent. The progress of labor may not cease after the rupture has occurred, and in some cases spontaneous delivery took place after the rupture. In the diagnosis of uterine rupture the history and external examination are of the greatest importance. The most efficient treatment for uterine rupture is an abdominal operation. Etiologic factors in uterine rupture are connective tissue changes in the uterus, especially the presence of scars and inflammatory changes.

J. P. GREENHILL.

Bazán, Julio, and Imaz, Francisco A. Uranga: The Treatment of Rupture of the Uterus, *Rev. españ. de obstet. y ginec.* 20: 454, 1935.

The writers report 21 cases of rupture of the uterus in 27,500 obstetric patients admitted to the hospital. Fourteen patients were cured and 7 died, 2 from peritonitis and 5 from hemorrhage and shock. Surgery was performed in 18 patients while three patients were treated conservatively. Hysterectomy was done in 13 cases and 2 cases were sutured. Two of the hysterectomies were done vaginally and one case was sutured from below. Of the 13 abdominal hysterectomies, 7 patients lived and 6 died of either hemorrhage, shock, or peritonitis. All patients operated upon vaginally lived. Patients' ages ranged from twenty-two to thirty-five years. All except three of the patients were multiparas with many children. Blood transfusions were done in only 9 patients, 7 of whom lived. The small number of transfusions was due to the fact that during the first few years of existence of the hospital, the blood transfusion department was not functioning. The writers agree that surgery and not expectant treatment should be the procedure to follow but that the patient must be prepared by transfusion, especially when there is shock—even if the operation must be delayed for a few hours. Suturing the uterus may be done in clean cases.

F. L. ADAIR AND J. SUAREZ.

Coutts, D.: Foetus Removed From Mother's Thigh Following Rupture of the Uterus, *Proc. Roy. Soc. Med.* 29: 308, 1936.

Under this striking title the following case is reported: A Hindu woman, thirty-five years old, was admitted to the Hospital for Women in Patna, India. A few hours previously she had been knocked down and run over by a heavy motorbus.

Outside of cuts and bruises on various parts of the body she showed enlargement of the lower abdomen and a swelling in the upper third of the right thigh. The latter swelling on palpation suggested the presence of fetal parts, and on questioning, it was ascertained that the woman had not menstruated for the last four months. Vaginal examination revealed an enlarged and soft uterus, tilted to the right. Cervix enlarged, soft, closed, no bleeding. To right extreme tenderness. Catheter urine clear. Pulse 86, small, easily compressible; respiration 37. Patient in profound shock and semiconscious. Appropriate measures against shock immediately taken. Next day patient was improved and swelling in thigh larger. An x-ray picture (presented in this report) confirmed palpatory findings, namely, a fetus with head down, lying in front of femur. With a vertical incision, extending up to the groin, the fetus was removed, lying just under skin and superficial fat in a bag of bloody fluid. The inguinal ligament was found detached at both its ends and the muscles attached to the anterior third of the right iliac crest were torn. Then incision was extended upward, following the cord, until the uterus was reached.

There was a rupture anteriorly, grasping the placenta which was extracted. Practically no bleeding. The structures below the deep fascia of the thigh were unaffected. Some blood in peritoneal cavity. Considering the patient in no condition for a hysterectomy, the uterine rent was stitched up like in a cesarean section. Within the abdomen a big rent, eight inches long, was felt running up to the costal arch. It was closed, after further lengthening the incision. Finally wound closed and two drainage tubes inserted through stab wounds. Recovery proceeded rather satisfactorily when patient, about five weeks after operation, on account of a terrific earthquake rushed outside in a heavy rain. She developed a pneumonia from which she recovered, finally was discharged in satisfactory condition.

The striking displacement of the fetus could be explained in two ways: (1) Bus struck her on the left, running over her, rupturing uterus and forcing fetus down into thigh; (2) blow and pressure were on the right, stripping skin and fascia off the thigh, they detached the inguinal ligament and abdominal muscles, tore the peritoneum and ruptured the uterus. On rebound, the contracting uterus squeezed the fetus under the skin of the right thigh along the line of least resistance.

HUGO EHRENFEST.

Frewer, Edward: *Twins With Doubly Knotted Cords*, Brit. M. J. 1: 159, 1936.

A case is reported of twins sharing one amniotic sac and showing an unusual development of the umbilical cords. Arising from the placenta was a single thick cord; $1\frac{1}{2}$ inches from the placenta it divided into 2 cords, one unusually thin, 25 inches long, belonging to the first child, the other of normal thickness 15 inches long. The thin and longer cord formed two knots by being looped and twisted about the thicker, shorter cord. Both knots were easily loosened, and no adhesions were present. The babies weighed 3 pounds 10 ounces and 4 pounds 5 ounces, respectively. The smaller of the two survived; the larger died after thirty hours with signs of cerebral immaturity.

F. L. ADAIR AND S. A. PEARL.

Coleman, J. Stanley: *Two Cases of Twin-Locking*, Lancet 1: 196, 1936.

Because twin-locking is so very rare, the author reports two cases of this condition.

The first patient was aged twenty-nine, gravida ii. After $28\frac{1}{2}$ hours of labor, the cervix was still three-fourths dilated. Under anesthesia it was fully dilated and above were two heads palpated, impacted at the brim. The second head was wedged under the chin, against the neck and upper thorax of the first fetus. The second head was liberated and displaced upward. The head of the first fetus was flexed, rotated and then delivered by forceps. Loops of cord were then discovered to be responsible for the extension. Because of moderate bleeding the second fetus was immediately delivered by forceps. The twins were binovular. The mother and twins had an uneventful recovery.

The second patient was aged twenty-seven, a primigravida, and was admitted to the hospital because of severe toxemia. The toxemia improved. Nineteen days after hospitalization the membranes ruptured spontaneously and labor ensued. After eighteen hours it was evident that a serious obstruction existed. An examination under anesthesia revealed a prolapse of a hand under the chin of the first fetus and the head of the second fetus was at the inlet. The second head was displaced and the first head was delivered by forceps. The second twin was delivered by forceps immediately.

In both of these patients the anesthesia and manipulations were carried out with the patient in the left lateral position. The author advises early interference before impactions become severe.

H. CLOSE HESSELTINE.

Constantine, M. C. E.: A Case of Quadruplets, *Brit. M. J.* 2: 1206, 1935.

Quadruplet pregnancy occurs once in 654,455 births, as calculated by Diddle and Burford from a total of 219,899,446 recorded births.

The author describes the case of a para iii, aged thirty-four, giving birth to four living boys, diagnosed antenatally by x-ray. The delivery was uneventful. Two babies presented as vertex and two by the breech.

The placenta was expelled in two portions. One larger mass consisted of two placentas joined by contiguous margins. One of these had one chorionic and two amniotic sacs; the attached one had a distinct chorion and amnion. The placenta, expelled separately, had a complete chorion and amnion. Hemorrhage was not excessive.

The infants weighed 3 pounds 7½ ounces, 2 pounds 2½ ounces, 3 pounds 8½ ounces, and 3 pounds 10 ounces twelve hours after birth. First born died three days later as result of atelectasis of lungs and a patent foramen ovale. The second baby died on the sixth day, showing atelectasis at postmortem. The mother's puerperium was normal.

F. L. ADAIR AND S. A. PEARL.

Items

American Board of Obstetrics and Gynecology

The next written examination and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology will be held in various cities in the United States and Canada on Saturday, March 6, 1937.

The next general examination for all candidates (Groups A and B) will be held in Atlantic City, N. J., on June 8 and 9, 1937, immediately prior to the American Medical Association meeting.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for these examinations must be filed in the Secretary's office not later than sixty days prior to the scheduled date of examination.

Central Association of Obstetrics and Gynecology

The Eighth Annual Meeting of The Central Association of Obstetricians and Gynecologists was held in Detroit, October 15, 16, and 17. The guest speaker was Dr. Emil Novak of Baltimore. The following officers were elected for the coming year:

President: Dr. Jean Paul Pratt, Detroit.

President-Elect: Dr. Robert D. Mussey, Rochester.

Vice-President: Dr. Calvin R. Hannah, Dallas.

Secretary-Treasurer: Dr. Ralph A. Reis, Chicago.

Asst. Secretary: Dr. William F. Mengert, Iowa City.

Dallas was chosen as the meeting place for 1937.

Correspondence

Inquiry on the "Safe Period," by the National Committee on Maternal Health, Inc.

To the Editor:

In line with our interest in "medical aspects of human fertility," we are impressed by the extensive and increasing interest in and reliance upon the so-called "safe period" as a means of contraception. There is urgent need for determining, as accurately as possible, whether there exists, for the regularly menstruating woman, a predictable and reliable moiety of her cycle in which fertilization is impossible. The National Committee on Maternal Health is undertaking to collect pertinent data which, by reason of their source, will be of exceptional value. The cooperation of the medical profession is invited for this investigation.

We seek to enlist specially qualified married couples who will scrupulously keep and transmit to us—through their doctors and, of course, confidentially—accurate and complete records of menstruation and coitus over a long period of time, several years if possible. We hope that physicians reading this journal may, directly or indirectly, enable us to receive the cooperation of suitable couples, of whom one or both are, say, physicians or graduate students or faculty members or research workers in biologic or other scientific departments, therefore competent to furnish trustworthy records and also scientifically interested in contributing to this investigation.

A couple such as we wish to enlist might prefer not to have a pregnancy develop during the next year or more, although if one did develop it would not be calamitous. Accordingly the couple would observe the so-called "safe period" as their sole means of avoiding conception. If that succeeds, and then the time comes when they desire a child, they would reverse their practice, confining coitus to occasions outside the "safe period," or they would at least restrict intercourse to the moities of the menstrual cycle when, theoretically, pregnancy is most likely to result, and then record how soon it does result. Needless to say, there must be no known or probable factor of involuntary sterility in either one of the couple.

The frankly experimental character of the coital practices upon which these records are based, and the special qualifications of the recorders, will make these data uniquely valuable.

The Committee is peculiarly fitted to collect these records. Its territory is large enough to encompass couples in number adequate for the investigation—couples who, by reason of their particular qualifications and their willingness to volunteer, must be few in any one community, no matter how large the latter may be.

Upon application, we shall be glad to furnish to physicians simple record forms and brief instructions easy to follow which they may distribute to cooperating patients. We hope to hear from as many as possible who are reached by this announcement. Please address: National Committee on Maternal Health, Inc., New York Academy of Medicine Building, 2 East 103rd Street, New York, N. Y.

—RAYMOND SQUIER, M.D.
Executive Secretary.

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